SCRUB TYPHUS INVESTIGATIONS IN S.E. ASIA

REPORT ON INVESTIGATIONS BY G.H.Q. [INDIA] FIELD TYPHUS RESEARCH TEAM, MEDICAL RESEARCH COUNCIL TYPHUS TEAM

Based on

SCRUB TYPHUS RESEARCH LABORATORY

S.E.A.C. IMPHAL.

PART I

GENERAL REPORT

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WAR OFFICE
MARCH 1947.

SCRUB TYPHUS INVESTIGATIONS IN SOUTH EAST ASIA

A Report on Investigations on Scrub Typhus by the G.H.Q. (India) Field Typhus Research Team, and the Medical Research Council Field Typhus Team, based on the Scrub Typhus Research Laboratory, South East Asia Command.

PART I: GENERAL ACCOUNT

Army Medical Directorate
The War Office
March 1947

SCRUB TYPHUS INVESTIGATIONS IN SOUTH EAST ASIA

FOREWORD

1. The Scrub Typhus Research Team, based on Imphal near the Indo-Burma border, comprised a G.H.Q. (India) Field Typhus Research Team (Major S. Lal Kalra, IAMC, Pathologist, in charge), together with R.A.F., Friends Ambulance Unit and Civilian members, selected by the Medical Research Council, and all attached to a South East Asia Command unit known as the Scrub Typhus Research Laboratory.

The growing team started a programme of systematic field work in April, 1945. The whole team was working together from July to December, after which its numbers rapidly dwindled, and all investigations by the skeleton team stopped by the end of March, 1946, when the two remaining officers and their assistants finally left Imphal.

Work on the findings was not properly resumed until August, 1946, at the Department of Entomology, London School of Hygiene and Tropical Medicine.

2, The deferment of release from the Army of Lieut Colonel J. R. Audy, formerly officer in charge of the Scrub Typhus Research Laboratory, was extended into 1947 in order to enable him to complete the present Report, the form of which was decided by the following factors:

(a) The premature dissolution of the research team and the scattering of its members;
(b) the varied fields investigated and the present delays in publication, which would inevitably lead to the scattering of published papers in many different journals, making difficult the important task of integration later on;
(c) the existence of certain useful reports which however might never be rewritten for publication, and
(d) the fact that investigations were to continue, by the G.H.Q. (India) unit and by a small team to be based on the Institute for Medical Research in Kuala Lumpur, so that much useful information would not yet be ready for general publication.

3. The present Report accordingly presents both a review of Scrub Typhus in the South East Asia and India Commands, and an integration of the epidemiological investigations (Part I), supported by separate illustrated papers (Parts II and III) by individual workers, to which reference may be made for detailed study. It is the result of an attempt to prepare a comprehensive account, in some haste, of investigations which could not be properly rounded off; while the investigations themselves, carried out in the field, were partly of an emergency nature. For these reasons it suffers many defects and may compare unfavourably with the scientific thoroughness to be expected of a report on carefully planned work carried out under peace-time conditions.

Contents of the Present Report

THE OCCURRENCE AND IDENTIFICATION OF THE TYPHUS GROUP OF FEVERS IN SOUTH EAST ASIA COMMAND

Written in 1945

by

M.H.P. Sayers, O.B.E., M.B. Lond.,
Colonel, R.A.M.C.,
Deputy Director of Pathology South East Asia Command,
and
I.G.W. Hill, C.B.E., F.R.C.P. Edin.,
Brigadier, R.A.M.C.,
Consulting Physician, South East Asia Command.

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The original of this paper has been reproduced without change, except for the addition of a few comments, and references to Appendices in Part III of this Report - J.R.A.

THE MEDICAL RESEARCH COUNCIL SCRUB-TYPHUS COMMISSION

By

Dr. R. Lewthwaite, O.B.E., D.M., M.R.C.P.,

Director, Institute for Medical Research, Kuala Lumpur,

Federated Malay States.

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By

Lieut. Colonel J. R. Audy, R.A.M.C.,

Scrub Typhus Research Laboratory,

South East Asia Command

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By

J. R. Audy, M.B., B.S., Lond.

Lieut. Colonel, late R.A.M.C., formerly Officer in Charge

Scrub Typhus Research Laboratory

South East Asia Command.

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THE OCCURRENCE AND IDENTIFICATION OF THE TYPHUS GROUP OF FEVERS IN SOUTH EAST ASIA COMMAND

The purpose of this paper is to place on record the occurrence, geographical distribution, epidemiological features and the results of certain laboratory investigations on cases of the typhus group of fevers, particularly of scrub typhus (tsutsugamushi fever *) encountered in the Eastern Theatre, in the years 1941-44.

Before the Japanese threat to India in 1941, fevers of the typhus group were relatively uncommon among Indian and British troops in India. The total number of cases for the army in India reported during 1934 was 108, of which 35 were undoubtedly OXK in type, (Boyd, 1935). In Burma and Ceylon, typhus was a medical curiosity (Kundu, 1932, Nicholls, 1940).

Outbreaks occurred among troops in Burma and Eastern India from 1941 onwards, and at one period of the Burma campaign scrub typhus ranked after malaria, as the most serious medical problem. Five thousand cases occurred in 1944, with some 350 deaths. The notable feature at first was the occurrence of a series of sharp outbreaks, with intervening quiescent periods during which few cases were reported. Thus there were outbreaks in Burma (Meiktila) in September 1941 (107 cases); in Calcutta in 1942 (20 cases); at Ranchi early in 1943 (33 cases); and at Jhingergacha near Calcutta in the following autumn (58 cases). The year 1943 closed with a sudden outbreak in a British regiment south of Imphal (121 cases) and an explosive outbreak in Ceylon, when over 750 cases were admitted to hospital within a week.

It was apparent from these early outbreaks that the disease showed a marked seasonal variation. This was corroborated by subsequent experience, and the second half of the year came to be known as the "typhus season". As operations spread in the later months of 1944, into the Kabaw valley and across the Chindwin, and down the 'railway corridor' in northern Burma, the incidence of the disease markedly increased and ceased to fluctuate widely. In August that year there were 800 cases and thereafter between 600 and 700 cases per month occurred regularly till the end of the year. Such figures had never previously been recorded.

Owing to the fact that military operations of some complexity were occurring throughout the period under consideration, considerable difficulties existed in collecting accurate figures for epidemiological analysis. The available data indicate only in broad outline the incidence of infection in the principal foci in Burma, India and on the Indo-Burma border. Table 1, and the Chart and Map, at pages 15 - 16 and overleaf, summarise the main outbreaks and indicate the numbers of cases and geographical location of the units involved. Table II indicates the mortality rates. Experience in Burma will first be described as a majority of the cases of typhus occurred either in this country or on the Indo-Burma frontier.

* The identity of scrub-typhus with the classical tsutsugamushi of Japan and Formosa is accepted. The term 'scrub-typhus' is used in this paper, since it obtained in war-time usage.

BURMA and the INDO-BURMA FRONTIER

The outbreak of 1941.*

This, the earliest of any importance to be described in the army, was reported by Gurbuxsh Singh (1945). In September 1941, 107 cases occurred in a rural area near Meiktila in Central Burma. Clinically the disease was scrub typhus and local necrotic lesions of the skin were observed in 36 per cent of cases. Serological tests showed agglutination of Proteus OXK to significant titre in 97 per cent of cases. Two patients died and the epidemic corresponded in all but mortality with the disease as later encountered. All but two of the patients belonged to one unit which proved to be infested with lice, and a company of that unit which was free from lice was also free from disease. These observations, coupled with the occurrence of weakly positive agglutination of OX19 suspensions in 16 cases, suggested to Gurbuxsh Singh that the louse was a possible vector, but no further evidence in support of this hypothesis was recorded.

The Burma Retreat 1942.

The extent to which fevers of the typhus group occurred during the retreat from Burma in the summer of 1942 remains unknown. Then and in the months that followed, medical officers were generally unfamiliar with this group of fevers, and laboratory facilities were lacking. After the fall of Burma, "typhus" was first recognised in stations where there were laboratories, such as Ranchi, Calcutta and Imphal.

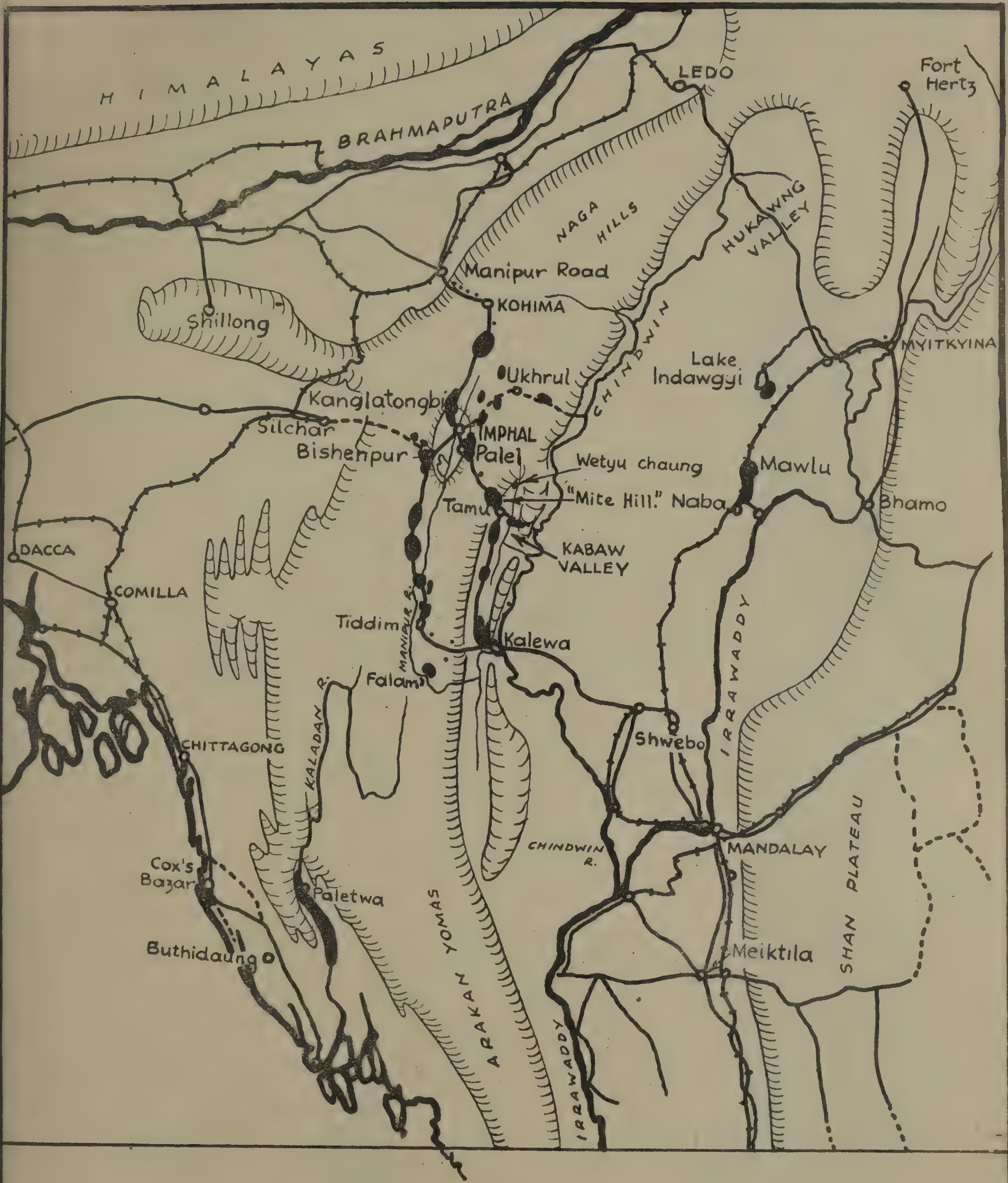
Manipur State and the Kabaw Valley, 1943.

In the first nine months of 1943 only some twenty cases, and these from widely scattered areas around Imphal, were admitted to hospital. In October and November of that year the first big outbreak of scrub typhus drew attention to the importance of this disease in future operations in Burma (Tattersall and Parry, 1945). On October 11th 1943, a battalion of a British regiment arrived from a non-endemic area and patrolled down the Tamu Road some 5 miles north of Moreh, in the hills above the valley of the Yu river. Two companies patrolled a certain hill feature, a ridge about 2 miles in length, the original jungle on which was replaced by rank grass, scattered stunted trees, and occasional young palms. On November 2nd. three weeks later, the unit left the area. Cases of scrub typhus began to occur on October 20th and continued until November 19th, 17 days after the unit left the area. The maximum daily incidence occurred from the 23rd to the 27th October, corresponding to an incubation period of 12 - 16 days. In all, 121 cases were reported, the majority of which occurred among the companies which had patrolled the ridge, later known as "mite hill".

App. 2 p.16.(2) (also see Addenda)

Figs. 2: 45, 46, 47.

* There is reason to believe that these infections were actually incurred not in the Meiktila area but south of Mandalay (? Myityngo-Kyaukse area) - see Appendix 2 p. 13, para 9(1) - JRA.



MAP SHOWING AREAS IN BENGAL, ASSAM & BURMA WHERE SCRUB TYPHUS WAS REPORTED IN 1944

MOUNTAINS

MAJOR ENDEMIC FOCI

MILES

0 25 50 75 100 125 150

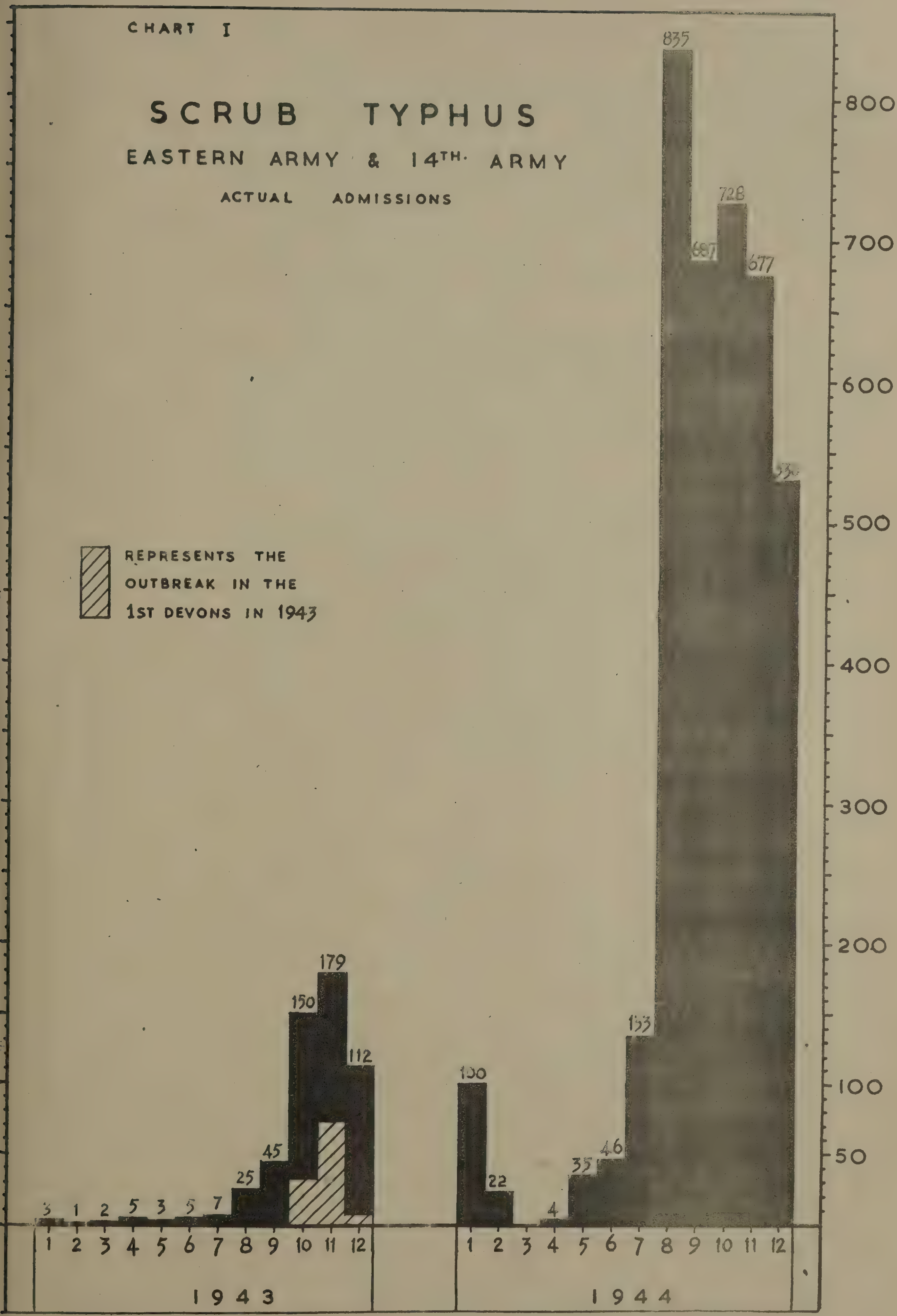


CHART I
SCRUB TYPHUS
EASTERN ARMY & 14TH. ARMY
ACTUAL ADMISSIONS
REPRESENTS THE OUTBREAK IN THE 1ST DEVONS IN 1943
3
1
2
5
3
5
7
25
45
150
179
112
100
22
4
35
46
133
835
728
677
1 2 3 4 5 6 7 8 9 10 11 12
1943
1 2 3 4 5 6 7 8 9 10 11 12
1944
50
100
200
300
400
500
600
700
800

This outbreak was the subject of detailed clinical and pathological studies, referred to in the second part of this paper, which fully confirmed that the disease, hitherto commonly known as scrub typhus, differed in no essential particular from tsutsugamushi fever. (During the dry season about 3 months after the outbreak, an extensive fire occurred on "Mite Hill". After the monsoon in August 1944, adults of T. deliensis were found in the soil of the burnt site.)

App. 2 p. 29 (Fig.45)

The Burma Fronts 1944.

On the Northern and Central fronts, cases occurred in appreciable numbers wherever troops were engaged, with the overwhelming majority among those operating along the roads and tracks radiating from Imphal. The Southern front (the Arakan) on the other hand, was almost free from scrub typhus until the operations in the valley of the Kaladan in November 1944.

A feature common to the regions where infection occurred, was the 'scrub' country, consisting of areas of rank grassy waste-land which resulted from old jungle clearings. The focal incidence of infection was demonstrated by the occurrence of isolated groups of cases from various areas along the tracks south of Imphal. It appeared that localised infected patches of ground existed within wide areas of waste-land and workers in this theatre have claimed that it is possible to pinpoint such highly localised 'islands'. The significance of these observations was explored in the hopes that the application of air-photography to the survey of typhus country might prove of value in assessing areas of maximum risk. (Lt. Colonel J.R. Audy, R.A.M.C., personal communication).

App. 4

An example, typical of many, illustrating the discreet localisation of infective foci was described to one of us (M.H.P.S.) by the officer commanding a field battery, which encamped for ten days on the banks of a small stream (chaung) in the Kabaw valley. The officers' lines were situated some 30 or 40 yards away from the main body. Seven cases of 'fever' occurred among the personnel occupying the officers' lines - three officers and four batmen - two weeks after arrival in the camp. In five of them, according to the officer commanding the unit, a diagnosis of scrub typhus was subsequently made. He himself contracted the disease twelve days after leaving the area, up to which time, he stated, no case of suspected scrub typhus was reported from the main body, although over 100 men had been engaged on jungle exercises. (All clothing had been treated with dibutylphthalate). Although there is little reason to doubt the reliability of this account, it was unfortunately impossible to confirm the details by examination of the clinical records of the patients.

(a) Central Burma Front. - From November 1943 up to the time of the withdrawal on to the Imphal plain the following March, some 240 cases were reported among troops operating down the roads leading to Tiddim and Tamu, South of Imphal. During the following two months, while the forces were con-

Maps 2: 4, 5

(a) (contd.)

centrated on the Imphal plain, no case was notified. With the raising of the seige in May, scrub typhus reappeared among patrols operating along the roads leading out of Imphal, and over one hundred cases were reported in May and June (1944) from this area.

There were few cases of scrub typhus among the troops advancing from Manipur Base (Dimapur) to the relief of Kohima in May. Only two cases were reported in the following month during operations to open the Imphal-Kohima Road. In July (1944) the incidence began to rise steeply as strong forces moved south of Imphal and nearly 200 cases were reported. In August over 700 cases occurred and this figure was almost equalled in September. The main foci of infection were along the tracks leading from Imphal to Ukrul and Bishenpur, the Tiddim and Tamu Roads and the valley of the Yu River. Operations in the Kabaw valley and towards the Chindwin resulted in nearly 1400 cases in October and November, and during these two months, over 100 further cases occurred among troops operating up and down the Imphal-Kohima road.

(b) <u>North Burma Front.</u> - Wingate's Special Force was flown into Northern Burma (north of Katha) in March 1944 and scrub typhus was not reported before May, when some 50 cases were flown out to hospitals in North Assam. Fifteen of these patients died. From enquiries from men of the force and from available accounts, it is probable that a number of men died of scrub typhus in Burma, before its occurrence was recognised. The foothills to the south and south-east of Lake Indawgyi were the most likely foci of infection. A few cases (11) also occurred in May among units of the Fort Hertz garrison while camping on the Myitkyina - Fort Hertz Road. Altogether between May and September 1944, 132 cases of scrub typhus were reported from the units of Special Force. In addition some 200 cases had occurred among American Forces operating further north near Shaduzup between March and May that year.

Special Force was relieved in July 1944 by a British division, and at first very few cases were reported as they advanced down the "railway corridor" towards Sahmaw. Only 18 cases were reported during August, and 33 the following month. Early in October, as operations proceeded south of Mawlu towards Pinwe, the incidence suddenly rose and during the last quarter of the year, 231 cases were admitted to hospital. The peak period was the latter half of November and December, after which the disease ceased as abruptly as it had begun. The following is taken from an unpublished report by the A.D.M.S. of the Division.

(b) (contd.)

App.2 p.18(14) "All these cases occurred between Mawlu and Naba, in a type of jungle which could hardly be called 'scrub'. It varied between tall trees meeting overhead and a certain amount of undergrowth, to thick, inpenetrable jungle as was encountered at Pinwe". There was no evidence to show that there ever had been any local populace on the main axis of advance and only a limited number of troops patrolled to outlying villages. In striking contrast to the earlier cases referred to above in the Wingate force, the mortality was only 2.6 per cent.

(c) South Burma Front. (The Arakan). Only a few cases of scrub typhus occurred among our troops in the Arakan during 1944. Under 30 cases were reported up to the end of October, including a small very localised outbreak in Cox's Bazaar. The valley of the Kalapanzin River, where the troops had been mainly operating, was thus not an infective focus. In November, however, as operations spread into the neighbouring valley of the Kaladan, nearly 100 cases occurred among the West African forces.

Enemy Accounts of Typhus in Burma.

It is highly probably that Japanese experience resembled our own, and that scrub typhus occurred among the enemy during their occupation of Burma. But from captured enemy documents it appears, curiously enough, that the Japanese did not recognise the disease as such. The most comprehensive account
App.1 p.2 described some 80 cases which occurred mainly in and around Mandalay in the Autumn of 1943. The clinical description sustained a diagnosis of scrub typhus. Serologically OXK
App.2 p.2 titres were low and of 44 results reported only 7 cases agglutinated this suspension significantly. Only one test for each patient however is recorded, and there is no note of the day of the disease on which it was done. The mortality was 7.4 per cent, and the gross post mortem findings were those of our Burma disease. The results of their animal experiments and the alleged finding of rickettsiae in liver and spleen smears from a fatal case have cast some doubt on the competence of the authors, who concluded that "the disease was a typhus-like illness which is identical neither with tsutsugamushi, epidemic typhus nor tropical typhus in its narrow sense." (Translation of captured enemy document.) It was also called by the Japanese "Burma eruptive fever".

After the Japanese surrender, Lieut.-Col. Hayakawa, of the Japanese Medical Service stated that he had later examined sera and guineapigs, inoculated from these Mandalay cases, at Singapore. He found high titres against OXK and established a strain of Rickettsia.

INDIA AND CEYLON

The Ranchi Outbreak of Early 1943.

Thirty three cases of typhus-like fever occurred among British troops engaged in jungle training near Ranchi in the early weeks of 1943. The clinical features closely resembled those of scrub typhus and were described by Bowes (1943). Serologically, the majority of these cases belonged to the indeterminate group, with agglutination of two or more Proteus strains. They thus differed from any series which has been met further east. (See Table 1.)

Typhus in the Calcutta Area 1942-43.

Fevers of uncertain origin, conforming to clinical descriptions of scrub typhus, had been reported from the Calcutta area as far back as 1912, when Bradley and Smith (1912) first suggested a diagnosis of "typhus" for an isolated case. No cases had been reported from this area however, for nearly twenty years before the outbreak of war. Cases of "typhus" in the army were notified from June 1942 onwards. They could App.9
be divided into two groups viz. sporadic cases occurring throughout the year and a series of unit outbreaks of varying size confined to the second half of the year (Parker, 1944). Two examples of the latter are described, (see Table 1). In the autumn of 1942, 16 cases occurred in a British battalion stationed in Calcutta. Eight of the patients were living in a large building in a densely populated part of the town. With the exception of one, a patient from Ranchi, all cases showed well marked agglutination of OXK, and all were clinically similar to those seen in subsequent outbreaks. There were 4 deaths. This was an instance of scrub typhus breaking out in the suburbs of a large town. Eleven cases had occurred under similar conditions the previous year among Greek sailors billeted in the same area. Sporadic cases during 1942 numbered 35. The largest unit outbreak occurred the following year under conditions more usually associated with scrub typhus. In the autumn of 1943, 58 cases were reported among troops operating near the village of Jhingergacha, about 80 miles from Calcutta. All except 3 were of OXK type. The area, which had been vacated by the local population, consisted of patches of cultivated land and bamboo clumps, which the troops had been engaged in clearing. Troops had occupied the site for several months before cases occurred.

A further 130 cases were reported from Calcutta itself during 1943. These were mostly isolated cases and scattered over many different units. Lusk (1945) has described the Jhingergacha series together with 54 sporadic cases he observed in Calcutta during the same period (June - December 1943). Clinically all cases from both series were similar and the majority agglutinated OXK. They differed from the later cases of scrub typhus elsewhere by absence of glandular swellings and local primary lesions. A rash was observed in only 9.6 per cent., but most of the patients were Indians, in whom slight

rashes would not have been readily seen. There were 17 deaths in all, giving a mortality rate of 14.9 per cent for the combined series. It is probable that a number of milder cases at Jhingergacha were missed before the true nature of the disease was appreciated.

In 1942 and 1943 among the sporadic cases, there were thirty three clinically indistinguishable from scrub typhus, but with predominent agglutination of proteus strains other than OXK, or with a mixed response (see Table 1). There was no fatality among these cases which occurred mainly during the second half of each year.

Ceylon and the Maldives.

A remarkable outbreak occurred in Ceylon early in
App.13 App.2 p. 19
January 1944. Over 750 cases of scrub typhus resulted from a four day exercise in December 1943, in a circumscribed jungle clearing in the southern coastal region of the island at Embilipitiya. The majority of the cases occurred among East African troops (713 cases) but 43 were among the British. This outbreak conformed in all but mortality (which was under 2 per cent) to the scrub typhus of Burma. Local primary lesions were noted in a high proportion (85 per cent).

App.14 App.2 p. 20, Figs.2:55 & 14:1

On the small island of Addu Attol (Maldive Islands) in the Indian Ocean, some 500 miles south-west of Ceylon, scrub typhus is endemic. From February to August 1944, 114 cases were recorded, which gave a figure of approximately 100 cases per 1,000 of the garrison per annum. No case was reported during the last four months of the year. This was almost certainly due to the fact that troops in the early months had been engaged in clearing gun sites, preparing ammunition dumps, slit trenches etc. These had, for strategic reasons, to be sited in scrub, regardless of the typhus risk. Once the work was finished, the incidence of the disease rapidly declined. The local inhabitants appear to be immune.

CLINICAL AND PATHOLOGICAL FINDINGS

An analysis of the signs and symptoms in a number of outbreaks in this Theatre has been made by British and American workers. In the vast majority of fevers where Proteus OXK has been agglutinated, the clinical features have been remarkably uniform, though variations have been recorded especially with regard to the incidence of adenopathy, primary lesions and rash. Tattersall (1945) has analysed 1,000 cases. His findings conform in all essentials to the classical descriptions of tsutsugamushi fever of the Japanese writers. Post-mortem appearances, though not sufficiently characteristic to be diagnostic, have also conformed to descriptions of this disease. Macdonald, working at the Central Military Pathological Laboratory at Poona, succeeded in demonstrating Rickettsiae in the endothelial cells of the precapillaries of the brain, from a fatal case from Imphal. These observations were confirmed by Lewthwaite, who considered the organisms morphologically indistinguishable from R. tsutsugamushi.

SEROLOGICAL OBSERVATIONS

The Weil-Felix Reaction.

The Weil-Felix reaction has not in our experience, been superseded as the simplest test for separating scrub typhus from other fevers of the typhus group and has proved technically satisfactory. Table I details a summary of the results of the Weil-Felix reaction in the early outbreaks. From this, it will be seen that in the majority of cases, agglutinins to Proteus OXK suspension appeared during the progress of the disease. In 1944 also, 91 per cent of sera from 2919 cases of typhus, were reported as agglutinating OXK in preponderence (Table III). App.18

Towards the end of the second week significantly raised titres (in excess of 1/125) of agglutinins were usual but peak readings were not encountered until the third week, after which titres again fell to reach normal levels by about the eighth week or later. Titres of 1: 10,000 (OXK) were found on several occasions and one of 1: 64,000 was encountered once though figures in excess of 1: 5000 were relatively uncommon. An occasional case diagnosed as typical scrub typhus on clinical grounds, gave a negative Weil-Felix response.

In a minority of cases, agglutinins to OX2 or OX 19 or to both, either separately or in addition to OXK occurred, though not usually in titres high enough to cause confusion. During 1944, 9 per cent of the 2,919 cases examined gave reactions according to the following three groups (see Table III):-

1. Cases with a predominant titre against OX2 (2 per cent)
2. Cases with a predominant titre against OX19 (3 per cent)
3. Cases with a mixed agglutinin response to two or more suspensions (4 per cent)

In the outbreak reported from Ranchi (Bihar) in 1943 the majority of cases agglutinated OX19 and OX2 to high titres. In Calcutta, cases with a predominant OX19 response occurred sporadically and the existence of such serological varieties of typhus in India is of course well known (Boyd 1935).

Sera of different titres were selected from cases of the first outbreak at Imphal and submitted to laboratories in India and elsewhere for confirmation. Reports on 11 sera examined in the United Kingdom (Army Emergency Vaccine Laboratory), Washington (The National Institute of Health, Bethesda) the Cairo (Central Pathological Laboratory M.E.F.), were in general agreement with our field laboratory results (see Table IV).

Rickettsial Agglutination

Rickettsial agglutination tests using antigens prepared from louse-borne and flea-borne strains of typhus, were carried out by the Army Emergency Vaccine Laboratory (through the courtesy of Major-General L.T. Poole) and by Major C.E. van Rooyen, R.A.M.C. at Cairo. Unfortunately it has been impossible hitherto to prepare a suspension of R. tsutsugamushi, with which agglutination tests can be performed.

In all, eight sera from typical cases at Imphal were examined. Van Rooyen found that agglutination, described as 'slight' occurred to a titre of 1 in 400 against a strain of flea borne typhus in one of the three sera submitted to him. All five sera examined at the Army Emergency Vaccine Laboratory, showed only traces of agglutination in low dilution against one or other antigen prepared from louse-borne and flea-borne strains. The highest titre observed was a 'trace' of agglutination against a louse-borne strain in a dilution of 1 in 80 which occurred in one case. The results are given in Table IV. It was concluded from these results that "the low titres obtained and the poor quality of agglutination did not suggest any antigenic relationship between the OX19 and the OXK groups of typhus". (Report from the Army Emergency Vaccine Laboratory 1944).

Rickettsial Complement Fixation Tests

Complement fixation tests were carried out on eight sera, also taken from Imphal cases. Five were examined at the Army Emergency Vaccine Laboratory, where only louse-borne and flea-borne strains were used in the preparation of antigens. These sera failed in all cases to fix complement with these antigens in the lowest dilution tested (1 in 5).

Three sera were examined at the National Institute of Health, Bethesda, using antigens prepared from louse-borne typhus, flea-borne typhus, Rocky-mountain spotted fever and scrub typhus strains. The scrub typhus strain, originally isolated from a case in New Guinea, was that known as the 'Karp' strain, which came into prominence in connection with the preparation of the lung-tissue vaccine against scrub-typhus, later to be used in this Theatre. * All three sera examined fixed complement to high titre with the antigen prepared from the 'Karp' strain. Results were uniformly negative with all other antigens(See Table V). From these results it was concluded by Topping (1944) that the Imphal cases were "immunologically closely related to those occurring in New Guinea and called 'scrub typhus'.

ANIMAL EXPERIMENTS

In December 1943, an appeal was received from the
App.18 American Typhus Commission then in Cairo, for strains of *Rickettsia* from scrub typhus cases. At that time no such strains were being maintained in India or the United Kingdom. In December 1943, Major Parker working in Calcutta, succeeded in demonstrating scanty rickettsial bodies in guinea pigs inoculated by one of us (M.H.P.S.), with ground blood clot taken from cases at Imphal, and had produced a specific iridocyclitis in rabbits by injection of infected guinea pig peritoneal fluid into the anterior chamber of the eye. At about this time we were fortunate in obtaining the assistance of Dr. S.R. Savoor, who had collaborated with Dr. Lewthwaite in pioneer work on scrub typhus in Malaya. Following the same technique (Lewthwaite and Savoor 1936) Parker and Savoor

* An account of field trials of the vaccine, giving inconclusive results because of the low incidence of scrub typhus encountered during the trials, is published by Card, W.I. & Walker, J.M. (1947): "Scrub Typhus Vaccine - Field Trials in South East Asia." Lancet, 1 (13): 481. - JRA.

readily established strains from the Imphal and Calcutta cases in rabbits and white mice, by passage from guinea-pigs inoculated intraperitoneally with human blood drawn early in the disease. The virus was also established in the rabbit by inoculation of infected human blood direct into the anterior chamber of the eye. It was thus possible to meet the request of the American Typhus Commission, to whom strains were despatched in rabbits, early in January 1944. There was no difficulty subsequently in establishing strains from all the main outbreaks by the same procedures. Representative strains from the Burma border (Imphal cases) and Bengal, were despatched for further study to van Rooyen at Cairo, where after further passage, they were sent to the United Kingdom. Strains have also been sent in white mice to Dr. Craigie in Toronto. From reports by Parker (1944) Lewthwaite and Savoor (personal communications to M.H.P.S.) the strains isolated were indistinguishable in their experimental pathology from those isolated from scrub typhus elsewhere and known as R. tsutsugamushi. Van Rooyen and Danskin (1944) transmitted the infection to Egyptian rodents, using the gerbille and Jerboa, in which the appearance of the organism was stated to be identical with that described by Lewthwaite and Savoor (1936) in Malayan scrub typhus.

DISCUSSION

The widespread occurrence of scrub typhus in the Eastern Theatre is one of the most notable features of the medical history of the recent war. The experiences in Burma described above have been similar to those of the Australians and Americans in the Pacific Theatres.

It appears that the disease has existed "silently" in widespread areas in this part of Asia, as a rickettsial infection of mites and their rodent hosts, (Lewthwaite 1945). App.2 p.38. App.9 p.4. The sudden invasion of these areas by men in unprecedented numbers, has led to the partial supplanting by man of the rodent as a host, with the consequent flare-up of the human disease. Thus scrub typhus may be said to be essentially an "occupational" disease, and cases occur only when circumstances require man to enter such infected areas. In climates such as those of Malaya and Addu Atoll, where there is no marked wet and dry season, cases occur throughout the year. In monsoon climates such as that of Burma, the risk of entering infected areas is associated with the rainy season. The reason for this is probably connected with factors associated with the life cycle of the mite and evidence from current work of the Scrub Typhus Research Laboratory in South East Asia, indicates that the density of the mite population on rodents trapped in infective areas near Imphal, is significantly higher in the wet than in the dry season (personal communication to M.H.P.S. from Lt. Col. Audy, R.A.M.C.). App.3 p.5 Fig.3:1,3

The frequent suggestion that the Japanese invasion was responsible for the spreading of the infection is untenable, because the disease has occurred in many localities which have not been occupied by the enemy.

From the investigations carried out on cases of the OXK serological type in different epidemics in this Theatre, this disease appears to be identical with tsutsugamushi fever. As far as is known there are no essential differences clinically or serologically between tsutsugamushi disease and scrub typhus as found elsewhere.

The precise nature of the other serological types of typhus-like fevers found in this Theatre is obscure. They have formed a small and numerically unimportant minority of the cases reported, and have occurred sporadically throughout the greater part of the area. By analogy with descriptions
App.15 of typhus-like fevers elsewhere, it may be assumed that the cases with a preponderating agglutination of OX19 are probably endemic murine flea-borne typhus, while those with a mixed response probably belong to the same group as one form of endemic typhus that occurs in Southern India, which may in fact be a member of the tick-borne Rocky Mountain Spotted fever group. Cases with a predominant OX2 response probably also belong to the same group and do not form a separate entity. A recent report on the results of complement fixation tests carried out on sera from three cases of the indeterminate group, seen in Mysore, indicate that such cases are immunologically similar to the Rocky Mountain Spotted fever group (Topping, Heilig and Naidu 1943).

While the typhus group of fevers of Eastern India and Burma can be readily grouped according to the predominant Weil-Felix response, it is curious that conclusive direct evidence for the incrimination of the various insect vectors concerned in these diseases, is lacking.*

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* Since this paper was written, more information has accumulated about the various arthropod vectors, including the isolation of a Rickettsia apparently of the Rocky Mountain spotted fever group from ticks in Manipur: Reference should be made to Appendix 17 and to the discussion of the typhus group of fevers in the epidemiological review contained in the present report. - JRA.

SUMMARY.

1. Outbreaks of scrub typhus in Bengal, Assam, Burma and Ceylon during military operations in 1941 - 44 are described.

2. Their relationship to season and terrain and the striking focal nature of infective localities are discussed.

3. The clinical features of the disease as described by various workers and confirmed by the authors' experience are indistinguishable from those of tsutsugamushi fever of Japan as described in the literature.

4. Serological studies showed a predominant OXK agglutination in the great majority of cases. The significance of the agglutination of other suspensions is discussed.

5. Rickettsiae demonstrated in the brain of a fatal case of scrub typhus, were pronounced indistinguishable morphologically from R. tsutsugamushi by competent observers.

6. A study of rickettsial agglutination did not suggest any antigenic relationship between the OX19 & OXK groups of typhus.

7. Rickettsial complement fixation tests confirmed that the scrub typhus on the Indo-Burma border is immunologically closely related to the scrub typhus of New Guinea.

8. Strains of Rickettsiae have been isolated from cases occurring in Calcutta, Imphal, Ceylon and Burma. Laboratory investigations of strains from Calcutta and Imphal, both in India and the United Kingdom, have shown them to be indistinguishable from R. tsutsugamushi.

9. It is considered that clinically, serologically and bacteriologically, the scrub typhus of this Theatre is identical with the classical tsutsugamushi disease.

ACKNOWLEDGEMENT.

We are much indebted to the many medical officers of South East Asia Command, too numerous to mention individually by name, for their co-operation in this study, and especially to Dr. Janet Niven, Dr. Norman H. Topping, Dr. R. Lewthwaite, Dr. S.R. Savoor, Lt.Col. C.E. van Rooyen and Lt. Col. J. R. Audy.

Our thanks are also due to Major General W.E. Tyndall, CBE, for his encouragement, to Col. C.H. Stuart-Harris, for valuable suggestions in arrangement of this paper, and to Major General T.O. Thompson, CBE, whose breadth of vision in the early days of the Burma Campaign stimulated researches at home and abroad, the results of which have done much to further our control of scrub typhus.

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TABLE I.

SUMMARY OF MAIN FEATURES OF OUTBREAK OF "TYPHUS" FEVERS IN 1942 - 44.

Country	Date	Area	Geographical features	Approx Nos of troops at risk	Month	Number of cases (Approx)	Cases with predominating titres: OXK	Other strains
BURMA & INDO-BURMA BORDER	1941	Meiktila	Grassy scrub	Battalion	Sept.	107	97%	
	1942	Unknown						
	1943	"Mite Hill" (Nr. Tamu).	Abandoned clearings	Battalion	Oct-Nov.	121	100% of sera tested	
CENTRAL FRONT	1944	Roads radiating from Imphal to Tiddim - Tamu Ukhrul and Kalo valleys.	Abandoned clearings and riverside scrub in mountains and valley-plains.	2 Corps.	Nov 43 - Mar 44.	240		
					May-June	100		
					July	200		
					Aug.	700		
					Sept.	700		
					Oct-Nov	1400		
					Dec	450		
					Total	3790		
	1944	Lake Indawgyi Myitkyina	Abandoned clearings and riverside scrub.	Division (Wingate's)	May-Sept	132	Over 90%	
NORTHERN FRONT	1944	South of Mawlu	Clearings, stream-side scrub, possibly also dense jungle.	Division	Aug.	18		
	1944				Sept.	33		
					Oct-Dec	231		
					Total	282		

Country	Date	Area	Geographical features	Approx Nos of troops at risk	Month	Number of cases (Approx)	Cases with predominating titres: OXK	Other strains
SOUTHERN FRONT	1944	Arakan: Kaladan Cox's Bazaar	River valley and abandoned clearings in low hills.	Division 2 Battalions	Nov -	130) 14)	Over 90%	
INDIA	1942	Calcutta	Urban and sub-urban waste-land.	Battalion	March-Dec Aug-Nov	35(Sporadic) 22(Unit outbreaks)	80%	10.5%
	1943	Calcutta	ditto	Brigade	All year June-Dec	108(Sporadic) 22(Unit outbreaks)	73%	20.7%
	1943	Jhingergacha (near Calcutta)	Waste-land among paddy villages	Brigade	June-Dec	58	95%	5%
	1943	Ranchi	Waste-land near foot-hills.	Battalion	Jan	33	Nil	nearly 100%
CEYLON	1944	Embilipitiya	Abandoned clearings	Division	Jan	756	Majority of Sera tested	Nil
MALDIVES	1944	Addu Attol	Scrub within coastal fringe of palms.	2 Battalions	Feb-Aug	114		

MORTALITY OF SCRUB TYPHUS IN FOURTEENTH ARMY 1944

TABLE II

Month	Total Cases	Total Deaths	Case Mortality per cent by Categories.			
			Total	B.O.Rs.	I.O.Rs.	E.A.O.Rs.
January	100	3	3	2.6	2.1	Nil
February	21	2	9.5	-	22.5	Nil
April	3	2	66.6	-	-	Nil
May	35	3	8.6	40.0	4.5	Nil
June	46	2	4.4	-	7.7	Nil
July	133	26	19.5	20.2	18.2	Nil
August	835	81	9.7	19.5	7.6	4.3
September	687	80	11.64	18.9	9.26	12.55
October +	528	60	11.75	10.37	13.08	7.15
TOTAL 9 MONTHS	2,388	259	11.29	12.76	9.32	7.91

+ Incomplete.

TABLE III

ANALYSIS OF POSITIVE WEIL-FELIX TESTS CARRIED OUT IN LABORATORIES OF FOURTEENTH ARMY IN 1944.

	PREDOMINANT TITRE AS SHOWN			
No. of Cases	OXK	OX2	OX19	Mixed
No. of Cases	2674	54	72	119
Per cent (Approx)	91	2	3	4

TABLE IV

Results from Agglutination tests using Proteus Rickettsial antigens, carried out in different laboratories on sera from cases from the Indo-Burma border.

	Imphal Laboratory (Parry)		Cairo Laboratory (van Rooyen)				
	Antigens		Antigens				
	OX19	OXK	OX19	OX2	OXK	Epidemic Rickettsiae	Murine Rickettsiae
Patient's name							
1. Gulbat Khan	25	10,000	50	50	6,400	-	400
2. Keen	0	5,000	0	0	6,400	-	-
3. McEltham	0	560	0	0	500	-	-

	Imphal Laboratory (Parry)		Emergency Vaccine Laboratory, United Kingdom				
	Antigens		Antigens				
	OX19	OXK	OX19	OX2	OXK	Epidemic Rickettsiae	Murine Rickettsiae
Patient's name							
1. Talbot	0	10,000	0	0	5,000	40 tr.	40 tr.
2. Bricknell	0	10,000	0	0	5,000	20 tr.	20 tr.
3. Foullae	0	2,500	0	0	1,280	20 tr.	20 tr.
4. Hodge	25	7,300	0	80	10,000	0	20 tr.
5. Bowditch	0	220	0	0	80	80 tr.	0

	Imphal Laboratory (Parry)		Washington Laboratory (Ida Bengston)			
	Antigens		Antigens			
	OX19	OXK	OX19	OX2	OXK	
Patient's name						
1. Nur Hussain	0	64,000	160	-	20,480	Rickettsial Agglutination not done.
2. Cotterell	0	40,000	0		20,480	
3. Wise	0	2,500	120	-	2,560	

TABLE V. Results of Complement fixation tests carried out at National Institute of Health, Bethesda, by Dr. N. H. Topping on Convalescent sera of cases from Indo-Burma border.

COMPLEMENT FIXATION TITRES.

Patients Name	Serial No.	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512	1/1024	1/2048	Weil - Felix OX-19	Weil - Felix OX-K
Cook Nur Hussain	10870											1:160	1: 20,480
Antigen:													
+ Rocky Mt. Spotted fever		0	0	0	0	0	0	0	0	0	0		
Endemic Typhus		0	0	0	0	0	0	0	0	0	0		
Epidemic Typhus		0	0	0	0	0	0	0	0	0	0		
Scrub typhus (Karp)		++++	++++	++++	++++	++++	++++	++++	++++	++++	++++		
Pte. Cotterell	2067330											0:	1: 20,480
Antigen:													
Rocky Mt. Spotted fever		0	0	0	0	0	0	0	0	0	0		
Endemic Typhus		0	0	0	0	0	0	0	0	0	0		
Epidemic Typhus		0	0	0	0	0	0	0	0	0	0		
Scrub Typhus (Karp)		++++	++++	++++	++++	++++	++++	++++	0	0	0		
Pte. Wise	5624329											1:120	1: 2,560
Antigen:													
Rocky Mt. Spotted fever		0	0	0	0	0	0	0	0	0	0		
Endemic Typhus		0	0	0	0	0	0	0	0	0	0		
Epidemic Typhus		0	0	0	0	0	0	0	0	0	0		
Scrub Typhus (Karp)		++++	++++	++++	++++	++++	++++	++++	++++	0	0		

THE MEDICAL RESEARCH COUNCIL SCRUB-TYPHUS COMMISSION

1. THE IMPACT OF SCRUB-TYPHUS ON THE ARMED FORCES IN S.E.A.C.

The decision of the Allied Command to invade Burma through its Western border, and to press the campaign through the monsoon period, was taken with the full realisation that casualties from tropical diseases would far exceed battle-casualties; it being confidently held that the Allied medical resources so surpassed those of the enemy that, whatever our losses due to tropical disease might be, those of the enemy would be much the greater.

That this realisation was well-founded was exemplified by the mounting incidence of an obscure tropical disease, Scrub-Typhus, which by the end of 1943 had become a major medical hazard to men and morale.

This acute infectious fever, of some fifteen days' duration, is caused by a germ, the Rickettsia tsutsugamushi, inoculated by the bite of larval mites which feed predominantly on wild rodents, especially rats. As a "silent" rural infection of mite and rat, it had in pre-war days rarely obtruded, for few were then at risk. But when troops in their thousands, as the tide of jungle warfare dictated, became of necessity exposed to the infected mites, supplanting the rat as host, the incidence of the disease soared, especially during the monsoon. Small outbreaks in "islands" of infected countryside studded combat and training areas. Notable large outbreaks that occurred at the outset of the projected campaigns of 1944-1946 alarmed medical and combatant commanders alike. As portents, they compelled attention and demanded counter-measures. The occurrence of 4,000 cases with 10 per cent mortality in the XIVth Army during the period June-December, 1944, brought early justification of this alarm.

The recognition that counter-measures, to be specific and timely, required instructed direction prompted the appeal for "specialist" aid by the Supreme Allied Commander, S.E.A.C., to the War Office in November, 1943. The problem came for review before the joint War Office-Medical Research Council "Typhus-Committee".

2. PREVIOUS RESEARCH

Scrub-typhus, as "tsutsugamushi" (i.e. "disease-mite") had long been known in Japan and China; in the former country the mortality-rate was 15-50 per cent. From 1879 onwards investigators in Japan and Formosa had recorded certain salient facts of its epidemiology and causal organism; Dutch workers in the Netherlands-Indies added more. In 1924 Fletcher and Lesslar at the Institute for Medical Research, Kuala Lumpur, first identified the disease in Malaya; their findings gave precision to its laboratory diagnosis with consequent great impetus to research on the disease throughout the Far East. Their successors at the same Institute elucidated its experimental pathology.

At the outbreak of the Japanese war there was thus a considerable sum of knowledge available, albeit disjointed, on which to plan further investigations and to devise counter-measures. Its broad distribution was defined, viz., an arc drawn on a map of the Far East, from Assam, through Ceylon, Malaya, the Netherland-Indies, Queensland, New Guinea, French Indo-China, Formosa to Japan; the clinical picture had been recorded; the nature of the causal organism was known, and its cultivation in laboratory animals had been satisfactorily established; the few attempts at vaccine preparation in Malaya had failed. There were, however, large lacunae in our knowledge of the epidemiology of the disease. And familiarity with the disease in ward, field and laboratory was

restricted to a few specialist workers, some of them captive in countries overrun by the Japanese.

When the imminence of war in the Far East necessitated the despatch of British forces to Burma and Malaya, the menace of this jungle form of typhus fever had not escaped recognition. In December, 1941, at a conference held in London between the War Office, the Medical Research Council, and Col. C.H. Kellaway, Director of Pathology, Australian Army, decisions were taken that resulted in Dr. R. Lewthwaite, Senior Pathologist, Institute for Medical Research, F.M.S., being flown from Singapore to Melbourne in January, 1942, taking with him the laboratory animals infected with scrub-typhus necessary for attempted vaccine production. During 1942-43 this work proceeded along lines then considered to be the most promising, viz, the cultivation of the virus of scrub-typhus in the yolk-sac of the fertile hen's egg, which had proved so successful in the hands of Cox in the U.S.A. in the case of the louse-borne, flea-borne and tick-borne groups of typhus fever.

3. ORIGIN OF THE SCRUB-TYPHUS COMMISSION

The response of the Typhus Committee to the appeal for assistance in S.E.A.C. was to despatch Dr. R. Lewthwaite to that theatre, as Field Director of a Scrub-typhus Commission, the original members of which were Dr. Kenneth Mellanby and S/Ldr. Charles Radford, R.A.F., both entomologists. Dr. Lewthwaite travelled to the United Kingdom from Australia by way of the United States of America, where he made valuable contact with American workers at the National Institute of Health and the U.S. Naval Medical Centre at Bethesda, and with the Rockefeller Institute in New York and the Walter Reed Army Medical School in Washington, all engaged in intensive research into vaccine production for scrub-typhus, in response to an appeal for assistance from General Douglas MacArthur's Headquarters consequent on a high and unexpected incidence of the disease in the island campaigns of the South-West Pacific theatre of war.

The Commission arrived at H.Q., SACSEA, in July, 1944.

It early became necessary to decide whether the three members of the Commission should restrict themselves to the propagation of known facts and counter-measures, or whether intensive and comprehensive research should be initiated in order to attempt to fill the many lacunae in our epidemiological knowledge. The latter view prevailed; for the impact of war had given special purpose to such research, and had provided a proving ground for whatever findings might ensue. Funds would not be lacking. A main field laboratory was therefore established at Imphal, to which H.Q. ALFSEA and G.H.Q. (India) contributed selected individuals.

For some months S/Ldr. C.D. Radford maintained a field laboratory on Addu Atoll, in the Maldive Islands, the scrub-typhus outbreak on which is described by Lt. Col. M.P. Sayers, O.B.E., elsewhere in this report. Collaborating with him was the G.H.Q.(I) Field Typhus Research Team commanded by Major S.L. Kalra, I.A.M.C. Page 7

In due course it became evident that this wide dispersion of available specialists was unprofitable; and the Addu Atoll laboratory was withdrawn and merged with the main laboratory at Imphal.

The complete staff was as follows:

Civilians:

Dr. Kenneth Mellanby - Deputy Field Director, Scrub-typhus Commission.
Dr. H. C. Browning * - Experimental Biologist.
Mr. K. Cockings - Friends' Ambulance Unit.
Mr. Gordon - Associate of Dr. Browning.

Service Personnel:

Lt. Col. J. R. Audy, RAMC - Military O.C. of the laboratory.
S/Ldr. C. D. Radford, RAF - Entomologist.
F/Lt. A. A. Bullock, RAFVR- Botanist.
Major H. M. Thomas, RAMC - Experimental Biologist.
Capt. H. C. Steward, RAMC - Administrative Officer and Quartermaster.

G.H.Q.(I) Field Typhus Research Team:

Major S. L. Kalra, IAMC - Pathologist.
Major M. L. Roonwal, IAMC - Deputy Director, Zoological Survey of India.

Technicians and General Duty personnel:

Twelve non-commissioned officers.

The premature cessation of hostilities was quite unforeseen when the decision was taken thus to broaden the range of activities of the Commission. However, the emergence from the laboratory work at Imphal of many interesting findings induced the military authorities to maintain the laboratory in the Imphal area until March 1946, some months after the area had been evacuated by troops.

4. THE SALIENT PROBLEMS CONFRONTING THE COMMISSION, AND THE ACTION TAKEN

These were twofold:

(i) Definition of the Precise Nature of the Disease

The typhus group of fevers comprises four main types, viz. louse-borne, flea-borne, tick-borne and mite-borne. Each would demand counter-measures peculiar to it; hence the importance of accurate and early identification in the present instance. Doubt was soon dispelled by the isolation in mice, guinea-pigs and rabbits of strains of the causal organism, the Rickettsia tsutsugamushi, by the inoculation of material from patients. This observation, made by Major M. T. Parker, RAMC, in Calcutta, and confirmed by Dr. S. R. Savoor, at once established the disease as scrub-typhus. Observations of the signs and symptoms in the patients were confirmatory.

App.8 (Parker)

In passing, it is of interest to record that the Japanese, who suffered thousands of casualties from this disease in Burma in 1943 and 1944, were at first completel[y] misled by it; in their perplexity they called it "Burma Eruptive Fever"; they considered it to be flea-borne, and recommended incorrect counter-measures in consequence. Not until the middle of 1944 did they identify it as their own tsutsugamushi disease.

Page 5

* A brief narrative of the recruitment of the staff of this ad hoc laboratory, by Lt. Col. J. R. Audy, is given elsewhere in this report. (Pages 55 to 58)

In due course field work by members of the Commission in infected areas, as far-flung as Imphal in Assam and Addu Atoll in the Indian Ocean, repeatedly and consistently recovered the known Malayan vector mite, Trombicula deliensis, from jungle rodents; some of these mites yielded strains of the causal Rickettsiae.

(ii) Application of Counter-measures

In their widest sense these included education, liaison with other research teams, mite-avoidance, and the application of such specific counter-measures as were known or could be evolved by immediate research in the field and base laboratories.

(a) Education: Whereas in the case of malaria the soldier was aware of the nexus between the disease and the mosquito, and seeing the latter he comprehended the occurrence of the former, in the case of scrub-typhus the situation was otherwise. The larval mite is minute, feeds for only three days, and causes no irritation; so that the victim is entirely unaware of having been bitten. The objective impression of the disease in the mind of the soldier was that formed by seeing first one, then another, of his unit carried down the line, with high fever and a cyanosed and drunken appearance; later he heard of the considerable death-rate, and was left with a depressing impression of a silent enemy against which he was helpless. That he frequently occupied foxholes lately vacated by Japanese suggested to him strongly that the disease was being deliberately "sown" by the retreating enemy.

To counter this psychological effect, an energetic campaign designed by lecture, film and poster to strip the disease of its imputed mystery was launched. A cine-film showing the life-history of the mite, its habitat, the technique of certain counter-measures, and other relevant features, was made under the direction of Dr. Kenneth Mellanby. The anti-malarial organisations were utilized to disseminate information as to those counter-measures known and in prospect. Frequent interviews and lectures at Army Headquarters at different levels were given with the same end in view.

(b) Liaison with other Investigators: At the time of the inception of the Commission, investigations of the many aspects of the scrub-typhus problem had already begun in various laboratories in India, Ceylon, the U.S.A., Australia and Great Britain. Of those concerned with the virus and vaccine production, more will be said below. Of those concerned with the vector, amongst the most important were those of the Australian entomologists, in the field by McCulloch and his team, in the laboratory by Womersley. In the autumn of 1944 Dr. Kenneth Mellanby and S/Ldr. Radford visited Australia and New Guinea, and there learned at first-hand the valuable progress made in the use of the mite-poison, di-butyl phthalate, referred to in more detail below. They made contact also with a team of American investigators in New Guinea.

Late in 1944 an American Scrub-typhus Commission, led by Colonel Thomas T. Mackie, M.C., AUS., established a field laboratory at Myitkyina, North Burma, in which area American forces were operating. By a interchange of visits the most cordial co-operation was attained

between the two Commissions.

Contact was also maintained with Mr. H. F. Carter, Government Entomologist, Ceylon, Dr. S. R. Savoor, of the Haffkine Institute, Bombay, and the G.H.Q. (India) Base Typhus Laboratory, Poona, all studying some aspect of the disease.

(c) Anti-Rat: Outbreaks of the disease have usually been associated with the presence of an abundant rat population. Obvious sites for camps or bivouacs are areas of secondary jungle, i.e. areas once cleared of primary jungle by the indigenous peasantry for the planting of grain or other crops, and abandoned by them when the fertility of the soil declined. Such areas become infested with rats, attracted by a ready food supply; and with the rats come their parasites, the mites. After feeding, the larval mites leave the host, and completion of the life-cycle takes place in the soil in the vicinity. Should either the rats or the larval mites be infected with the causal organism and the terrain permit the mite colony to thrive, the establishment of the area as a "scrub-typhus island" is assured.

Investigation made at the Commission's Imphal laboratory elucidated a point hitherto obscure, namely whether a larval mite, that owing to the death of its rodent host detaches when only partially fed, will at once undergo moulting to the harmless nymphal stage, or will first resume its feeding on another host, which in the case of a camp-site might well be man. It was found that larvae that had fed for less than one day prior to leaving their host would re-attach and continue to feed. Instructions that the killing of rats must be followed by immediate disposal of the rat and its attached mites by burning were accordingly issued in the field.

Earlier field work in Malaya had failed to reveal any practicable method of reducing the rat population of plantations, other than by unremitting organized rat-hunts. Success with poisons and "viruses" had been fleeting. It was not to be expected, therefore, that the scrub-typhus menace could be appreciably mitigated under campaigning conditions by schemes of rat-destruction.

(d) Anti-Mite: The counter-measures of this nature that were advocated fell broadly into two categories, mite-avoidance and the application of mite-poisons.

Mite-avoidance: There were many methods of proved worth. One, the use of local labour in the dangerous task of clearing scrub, rested quite securely on the observation in many known sites that indigenous populations are much less susceptible to scrub-typhus than are recent intruders; it is inferred, and is probably true, that attacks of the disease in early childhood, which are usually mild, have conferred an immunity. Others rested on the fact, and in degree are limited by the fact, that the larval mites prefer conditions to be humid, and will burrow into the soil should conditions become excessively dry. Thus the "civilizing" of an area by the cutting of paths, and by the strewing of such paths and tent floors with sand, will lead to a fall in incidence. The used of improvised hammocks, where feasible, was also effective. Bulldozing a camp-site would remove mites in proportion to the degree of thoroughness applied, and was a procedure much favoured by the American forces.

Mite-Poisons: The work of McCulloch and his colleagues in Australia on the evaluation of mite-poisons gave to us our most effective single weapon against scrub-typhus. Of the many substances tried, DDT, dimethyl phthalate and dibutyl phthalate, were the most promising. Uniforms impregnated with one or other of them were washed in different ways (with hot or cold water, with and without soap, etc.), and for a varying number of times; and were exposed to direct sunlight, to rain, to muddy water, and so forth. Under each set of conditions the "stopping-time" of those larval mites suspected to be vectors was observed. The conclusions of these observers were that all three substances poisoned mites; and that dibutyl phthalate, in virtue of its persistence in spite of six or seven washings, was the most effective.

Field observations established that by its use fully 75 per cent of cases could be averted.

A late observation by American workers in the Panama Canal Zone, and confirmed in the Commission's Imphal laboratory, was that the similar use of benzyl benzoate bid fair to be equally as efficient in the field.

(e) Anti-Rickettsial: Against the established rickettsial infection in man, penicillin and the chemotherapeutic agents, methylene blue and para-aminobenzoic acid, have entirely failed; the two latter in spite of very promising results in animal tests.

The development of a cotton rat lung vaccine has been described elsewhere. Its evaluation was prevented by the dramatically sudden ending of hostilities. Its application to the disease in the civilian population of Malaya, and in the greatly reduced armed forces in South-East Asia in the immediate post-war period is now under observation. The immediate effect of the cessation of jungle warfare, and of the decimation of labour forces during forced labour on the Siam-Burma railway, was greatly to reduce the incidence of this "occupational" disease; so that evaluation of the efficacy of the vaccine will be very protracted. That the vaccine would prevent the incidence of the disease was not to be expected; that it might reduce the death-rate was a reasonable expectation.

Fulton and Joyner (1945)

Card and Walker (1947)

This report would be incomplete were mention to be omitted of those laboratory and field workers who contracted the disease during 1942-1945.

Prior to 1939 only four recorded cases of laboratory infection with tsutsugamushi were known to the writer. They were in Japanese and Dutch workers; two of the four were fatal.

During 1942-1945 there were fourteen such cases that came to the writer's notice. Three were field workers, two of them members of the Commission's field laboratory in Imphal; all recovered. Eleven were engaged in laboratory "bench-work" in connection with vaccine production; three of them died of the infection, one in Melbourne, Australia, one in Bethesda, Maryland, U.S.A., and one in the Rocky Mountain Laboratory, Hamilton, Montana, U.S.A.

Six of the fourteen cases had been "vaccinated" against Scrub-typhus with a full course of the experimental cotton-rat

lung vaccine; all six recovered.

Eight of the fourteen were "unvaccinated", and it was amongst these that the three fatal cases occurred.

References

Card, W.I., and Walker, J.M.: Scrub-Typhus Vaccine - Field Trials in South East Asia. Lancet 1(13): 481, 1947.

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A REVIEW OF INVESTIGATIONS ON THE EPIDEMIOLOGY OF SCRUB TYPHUS IN SOUTH EAST ASIA

INTRODUCTION

(1) The Situation at the Beginning of Hostilities

The object of this review is to link into a consistent account what was known regarding scrub typhus at the beginning of hostilities, and the heterogeneous collection of findings discovered during the course of investigations by the team based on Imphal, near the Indo-Burma border. In order to preserve continuity, general statements are supported by marginal references to the various detailed papers contained as Appendices in Parts II and III of this Report, and certain sections are included in small type.

At the beginning of hostilities, casualties from scrub typhus were expected. It was known that Scrub Typhus (Tsutsugamushi disease, Flood Fever or Japanese River Fever) is apparently confined to South East Asia and the Pacific region, being an accidental infection of man by a rickettsia, _R. tsutsugamushi_ or _R. orientalis_, which is symbiotic in certain trombiculid mites and which produces a silent or 'inapparent' infection in the small mammals upon which the larval mites are parasitic.

Appendix 2:43(1,2)
Appendix 2:45(8)
Appendix 2:43(3) 2:44(6)
Appendix 2:44(4,5)

Scrub typhus was also known to be distributed in restricted foci, which the Japanese called _yudokuchi_ or 'noxious areas', and this tended to make scrub typhus an occupational disease, a feature of obvious and considerable military importance. Endemic foci were reported frequently to be in river valleys, to which they were indeed confined in Japan, whilst in Malaya scrub typhus was recognised to have a rural distribution, persisting in circumscribed areas of waste, grass-covered*, grazing grounds and in neglected estates, thus contrasting with the urban distribution of the flea-borne typhus. In Formosa, the disease was particularly frequent in valleys, near villages and plantations, and also apparently in forest, while in the nearby Pescadores, scrub typhus was "domestic" and confined to grassy patches in the native gardens. The occupational incidence in the latter fell on the native children, in the former on the adult males whose occupations of farming, foraging or fighting led them into contact with infected areas.

The disease was strictly seasonal in its distribution in Japan and Formosa, but this was apparently not so in Malaya.

Two major vectors of the disease were recognised, the mites _Trombicula akamushi_ (Brumpt) and _T. deliensis_ Walch, both so closely related that Gater (1930) suspected that they were forms of the same species. In addition certain other species of the same and other genera were suspected of carrying the disease, one of these (_Schöngastia schüffneri_ (Walch)) being definitely incriminated as an exceptional vector.

It was known that the larval mites alone were parasitic on small mammals, while the adults and nymphs were thought to be vegetarian, living in the soil and feeding on decaying organic matter or plant juices. It was also inferred that because the larvae fed but once, on lymph or the products of histolysis of the skin of their hosts, infection must therefore be transmitted hereditarily or "transovarially"+ from parent mites to their offspring, and in the case of _T. akamushi_ at least, this was proved to be so by Japanese workers. A similar situation was known to exist in the case of the rickettsiae of spotted fever in American ticks.

* _Lalang_ - a thatch-grass, _Imperata cylindrica_

\+ The word 'hereditarily' should imply concern with the chromosome mechanism, which is not the case, while 'congenital' should imply an event or feature more concerned with the process of development or birth. 'Transovarially', that is, through the egg when the egg is looked upon as a stage in the life-cycle and not as a spherical object, is favoured by the writer; it has been employed by the American writers in the past. 'Perovarially' would perhaps be more fitting etymologically.

Tsutsugamushi infection had been recovered from infested voles and rats in Japan and Malaya, and the locally prevalent hosts of the vector were generally considered to be reservoirs of the infection.

A major difficulty in the way of investigating the disease lay in the virus-like nature of the organism, which necessitated a troublesome laboratory technique and considerable experience for its establishment. That strains of R. tsutsugamushi differed slightly from place to place was suspected because of the locally varying incidence of primary lesions and other clinical features. A variety of vectors had been suspected for the same reasons.

This then was the situation at the beginning of hostilities. It was clear that a number of important lacunae in knowledge awaited attention.

(2) Early Problems

From the point of view of the epidemiologist in the Indo-Burma theatre, there were five major problems to be clarified.

(a) The exact identity of the disease in the war theatre required confirmation.

(b) Of the distribution of the disease, almost nothing was known which would allow even of guesswork in the anticipation of casualties, while its relationship to terrain was uncertain.

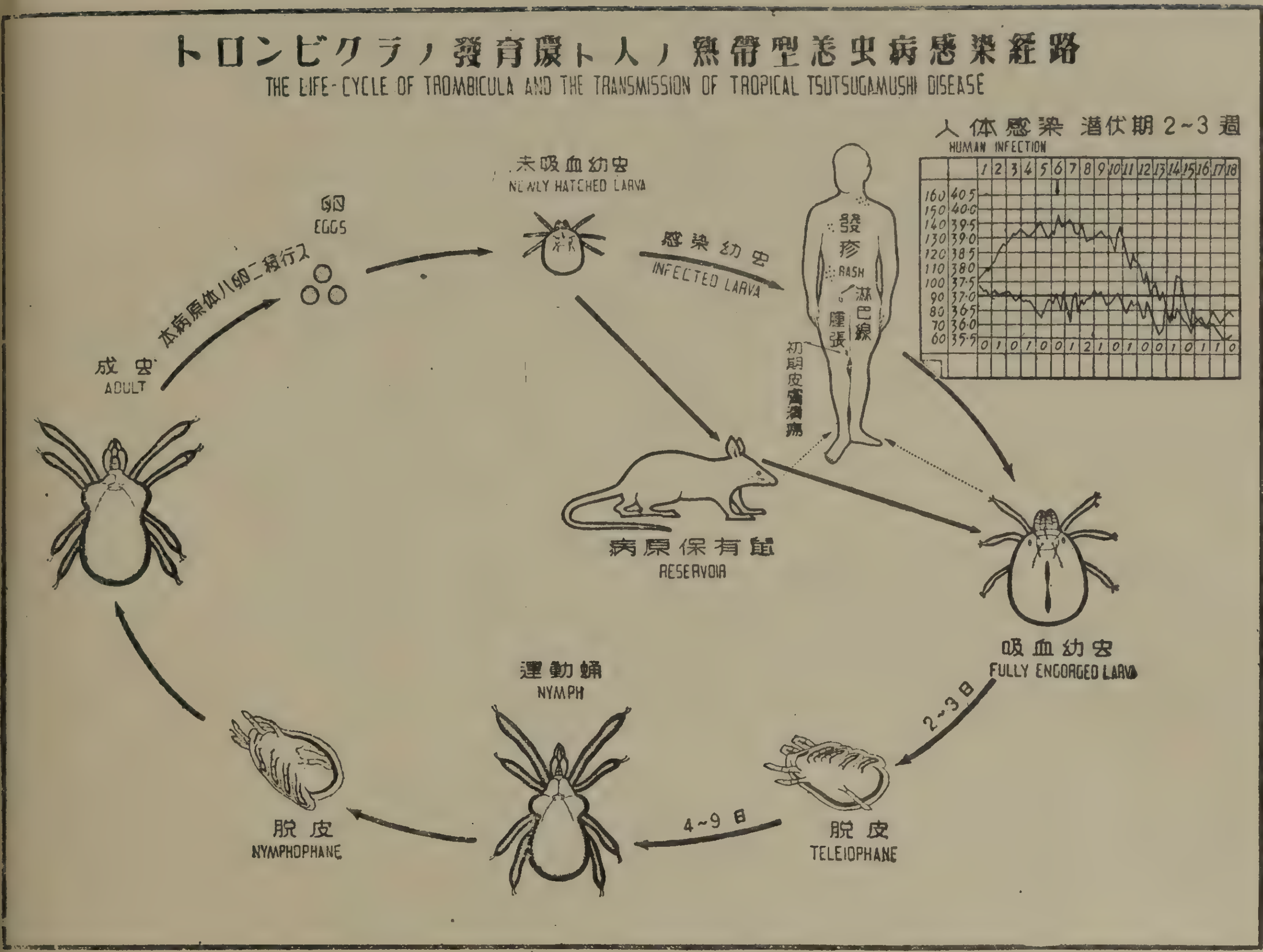
(c) The vector or vectors in the Indo-Burma theatre were not known. It was not even considered safe to assume that the vector was necessarily a mite.

(d) The bionomics of the mites had not been studied. The adults and nymphs were thought to be vegetarian, following Japanese workers, while almost nothing was known of the habitat of the vectors. Even the classification of the trombiculid mites was unsatisfactory and in an early stage of development, being based wholly on larval characters.

(e) The importance of rats and other small mammals as reservoirs was unknown, and all opinions rested on hypothesis. The species of rodent concerned in this theatre were unknown.

In the early stages of war-time investigations, the epidemiological picture became more confused, while the situation rapidly grew more serious. The chief lesson, dearly learnt, was the very wide distribution of the disease, and the heavy incidence in units which entered the endemic areas. Page 31 The disease was even encountered in areas which had previously been considered fairly free, such as Calcutta (see page 6 above) and Ceylon. Before 1943, scrub typhus had not been recorded from the Hambantota area of South Ceylon, while between 1936 and 1942 there was an annual average of only Appendix 13 9 cases of "Typhus", mostly murine typhus, over the whole of Ceylon, so that there was no reason to expect any hyperendemic centres there. Nevertheless, East African units of less than brigade strength on exercise in the Hambantota area in December 1943 occupied an Appendix 2:19(15) unsuspected endemic focus between two villages for just over four days, and suffered no less than 756 cases of scrub typhus in one week.

An increasing number of different vectors were described or suspected in the Pacific theatre. Even ticks had come under



THE LIFE CYCLE OF THE AKAMUSHI

From a captured Japanese account by Kiyosi Hayakawa, Lieutenant-Colonel, Medical Corps Japanese Army, formerly Assistant-Director, the Japanese Army Institute for Preventive Medicine, Singapore.

(dated February, 1946)

Note: The Life Cycle of the Akamushi

This illustration was inserted after the present Report had been completed. There had been no opportunity to add a review of the translated Japanese document of which the illustration was a part.

It must however be noted that the larva-nymph resting stage, which in the present Report has consistently been referred to as the 'nymphophane' is, in Hayakawa's illustration, named the 'Teleiophane', it is considered erroneously.

suspicion, while several new species of mite were described and shown to be vectors, but later found to be local representatives of either T. akamushi or T. deliensis.

Outbreaks were ascribed to a bewildering variety of terrain although many workers in New Guinea noted the particular incidence of the disease in patches of kunai grass* and in association with narrow belts of forest following watercourses and flanked by kunai, while the epidemiological features of the Ceylon outbreak had led the writer to suggest that a causal relationship exists between the occurrence of "typhus islands" of infection and primitive methods of cultivation, known as chena in Ceylon.

Appendix 2:19(15)

(3) A Summary of the Results of Subsequent Investigations

The investigations which are reviewed below have helped to fill these gaps in our knowledge, and they may be summarised as follows:-

(a) The disease in India, Burma and Ceylon had been identified as Scrub Typhus (Tsutsugamushi Disease) and strains of Rickettsia tsutsugamushi have been recovered from a number of areas, from patients, mites and wild rats, as described on page 7 above, and also in Appendices 8 (Imphal area), 12 (Assam-Burma), 13 (Ceylon) 16 (India) and 1 and 23(Burma)+.

Page 45 Appendices 1,2,4.

(b) The disease has been found to be widespread, and its patchy distribution related to ecological features in such a way as to allow constructive efforts to be made to estimate risk of infection by survey, including the study of air photographs.

Page32

(c) The vector has been established as Trombicula deliensis in all areas investigated in India, Burma, Ceylon and the Maldives.

(d) Studies on the bionomics of Trombicula deliensis have suggested that the following may be assumed:

Page 35

(i) The larval population of T. deliensis exceeds that of all other local species in endemic areas. The rate of turnover of T. deliensis greatly exceeds that of other local species and this is related to its success as a vector. T. deliensis is the major trombiculid ectoparasite of rats in the Oriental region.

Page 34(2)

(ii) T. deliensis and T. akamushi are apparently the only vectors of universal importance. They may be extreme forms of the same polytypic species, the chief member of a 'biologically successful' group of mites, the 'tsutsugamushi group'.

Page 32(2)

(iii) In monsoon climates, the larvae of T. deliensis have a seasonal incidence related to the presence of moisture.

Appendix 2:38 Photo 3:8

(iv) Certain perennially infested foci might act as centres of dispersal of both mites and disease.

* Kunai = lalang (Malaya) = Imperata cylindrica, a tall thatch-grass, which Japanese workers had suggested might be a source of food for larvae of T. akamushi in Japan.

\+ Also in N. Assam and N. Burma by the USA Typhus Commission (Mackie et al, 1946).

(v) The vectors and the disease have been encouraged by human activities connected with primitive cultivation, and scrub typhus may be broadly regarded as a "man-made" disease. Page 43

(e) The importance of the hosts (mostly murids but also shrews and squirrels) is two-fold: Firstly, their potentialities as reservoirs rest on the assumption (as yet unproved but for good reason generally assumed), that mites can pick up infection from infected rats. This still remains to be proved, but suggestive results have been obtained in an attempt to infect T. deliensis experimentally, while some important observations have been made on the course of infection in the principal host of T. deliensis in the Imphal area. Secondly, the manner in which the distribution and also the population of the vector mites are related to the numbers and the habitat of the hosts has been considerably clarified.

(f) A system of survey has been evolved which compares in its methods and purpose with malaria surveys. Practical points in field control have also emerged.

(g) Several techniques have been evolved which will be valuable to field workers.

GENERAL EPIDEMIOLOGICAL FEATURES OF THE JAPANESE CAMPAIGNS

Burma was re-entered along three wild and difficult routes: above the Chindwin into the apex of Burma, across the Chindwin through Manipur and the Naga Hills, and along the coast in the Arakan (Map 2:1). Each of these campaigns brought interesting epidemiological features to light.

(1) American and Chinese troops made and came down the Stilwell road from the Ledo railhead in North Assam to Myitkyina on the Irrawaddy, thence to the Burma Road. They had just over 1,000 recorded cases of scrub typhus (described by Mackie et al, 1946). Appendix 2:18 3:5(1e)

In the wet Hukawng Valley area no conclusive evidence was found that the incidence of scrub typhus was seasonal. The case incidence appeared to be related only to the movements of troops in and out of endemic foci. This is to be ascribed to the heavy perennial rainfall to be found over most of the valley, and appearances contrasted sharply with the dry-season fall in scrub typhus casualties further south.

(2) The main advance of Fourteenth Army was along the mountain passes in Manipur and the Naga and Chin Hills, through Imphal to Kalewa on the Chindwin, thence to Mandalay. There have been over 5,000 cases of scrub typhus in this area.

A striking feature was the intensity of the disease in units unlucky enough to strike endemic foci, as noted above, and an augury of this was the sharp outbreak in October 1943 at "Mite Hill" overlooking the Kabaw Valley, when the battalion occupying this feature suffered 121 cases of scrub typhus in three weeks. The record is probably held for this and other theatres by the 11th East African Division, which had over 1,600 cases in twelve months; 756 in Ceylon after a few days of exposure, and over 900 in the monsoon campaign down the notorious Kabaw Valley. Eighteen per cent of a single battalion (2nd West Yorks) on the Tiddim road got scrub typhus in two months, and in that time 5 per cent of the total strength had died of it. Page 29

A second feature was the heavy incidence in units on patrol or actively engaged with the enemy in 1944, contrasting with the preponderant incidence of "non-operational" typhus in Burma in 1945, when troops actively engaged escaped lightly.

A third feature was the marked seasonal incidence of the disease, which fell during the dry season and rose alarmingly during the rains.

Appendix 2:10 1:10 3:13-14

(3) The southern coastal route was through the Arakan. A most interesting point is that in the campaign through the Arakan Yomas*, although much exposure took place during jungle fighting, only one endemic region was encountered, along the narrow fertile valley of the Kaladan. This contrasted greatly with the very widespread endemic areas over ten thousand square miles of country west of the Upper Chindwin, and over almost the whole of Burma. There is some evidence that mountain ranges have formed an ecological barrier to the spread of scrub typhus, and it is suggested that the disease is infiltrating into the relatively non-endemic and shielded Arakan Yomas along the valley of the Kaladan, which has its source in the hyperendemic region near Tiddim.

Appendix 1:2

(4) Burma itself was overrun by the end of April in 1945, and there were about 600 more cases in Burma between June and December. At least 400 of these cases were "urban" or suburban in location, in the sense that they were within or on the immediate outskirts of villages and towns. Prome, Mandalay and Kalewa were the worst centres. Calcutta, Rangoon and Singapore have also proved to harbour endemic foci. It is now evident that much scrub typhus infection may be present in waste land in populated centres but remain unsuspected until unusual behaviour on the part of natives or of interlopers such as troops exposes them to the disease.

SALIENT FEATURES OF INVESTIGATIONS IN SOUTH EAST ASIA COMMAND

1. The Establishment of the Vector

The USA Typhus Commission established *Trombicula deliensis* as the vector in North Burma and North Assam, as well as demonstrating the transovarial transmission of infection in that species. A similar claim for the vector in Manipur, Assam, is also supported by the following evidence, while *T. deliensis* has also been found, on epidemiological grounds, to be the vector in Lower Burma, in the Kumaon Himalayas, the Jubbulpore area in Central India, and the Bangalore area in South India, as well as in Ceylon and the Maldive Islands.

(1) Geographical distribution of mites and scrub typhus. The two very closely related species *T. akamushi* and *T. deliensis* have the widest distribution of all the trombiculid mites, from North India and islands in the Indian Ocean to Queensland and Japan, and this corresponds to the distribution of the disease. The only species which appears to rival *T. deliensis* in extensive distribution is *Ascoschöngastia indica*, which, however, is not known to bite man and also was rare in the endemic areas around Imphal.

Appendix 3:10 Figs. 3:1,3,7.

(2) Seasonal incidence. In the Imphal-Tamu area in 1945, the seasonal incidence of larvae of *T. deliensis* was very marked and was followed very closely (Fig. 3:3) by the local case-incidence of scrub typhus. The case-incidence in Burma and Assam in 1944, and

* Yomas - mountain tracts

in Burma in 1945, also followed the same curve, and this seasonal incidence of the disease is fully established and cannot be correlated with the seasonal incidence of any other species of trombiculid mite.

(3) Dominant Mite Species in the infected areas. Trombicula deliensis has been found in every one of the many pin-pointed typhus "islands" so far investigated, usually as the dominant species. T. deliensis was also found to infest freely rats placed in situ in two very restricted infected sites, at Mile 24.5. on the Palel Airfield site, and at Mile 34 on the Palel-Tamu road. Appendix 2:3

(4) Biological factors. As will be seen later, T. deliensis has biological advantages over other species of mite, which alone are considered to establish its importance as a potential vector wherever it occurs.

(5) Infection of Mice infested by T. deliensis. In Mandalay, 5 mice exposed in a pin-pointed area by Dr. Browning became infected. From this same locality the only mites found on exposed mice were T. deliensis. Appendix 23:7 12:2

(6) Recovery of infection from T. deliensis. Strains established as Rickettsia tsutsugamushi have been recovered by Major Kalra from larvae of T. deliensis taken from the ears of wild rats.

Eight strains have been recovered from the following mites in the Indo-Burma area (Appendix 12 pp. 3 and 10):

(a) Two batches (250 and 300), apparently of larvae of T. deliensis alone, taken from rats' ears, from Mite Hill (Indo-Burma border) and Palel.

(b) Two batches of 14 and 20 larvae of T. deliensis during the course of an attempt to infect mites experimentally (see page 42 below).

(c) Four batches (60, 75, 100 and 300) of larvae of T. deliensis together with a small number of other species, also taken from rats ears, from Moreh (Tamu) and Palel.

The present position regarding the vectors of scrub typhus may be summarised as follows (Table 1). Other vectors have been suspected on general grounds and described in the literature, but these are unconfirmed.

It is however considered that the epidemiological picture appears in faulty perspective unless one examines the natural history of the disease rather than the mere accidental infection of man by one or two species of mite which happen to attack him. This aspect is elaborated below.

Table I: Carriers of Scrub Typhus to Man

Species	Recorded Distribution	Considered a Vector in:
T. akamushi	Japan Formosa Pescadores Philippines New Guinea S.W.P. Islands Malaya	Japan: A B C D (and transovarial transmission, and also probably infection in the adults, demonstrated) Formosa & Pescadores: A Philippines: A Malaya: A C S.W.P. and New Guinea A B D

Species	Recorded Distribution	Considered a Vector in:
T. deliensis	Philippines S.W. China New Guinea S.W.P. Islands Queensland Dutch East Indies Malaya Sumatra Burma India Ceylon Maldives	Sumatra: A B C Malaya: A (? with akamushi) Philippines: A B Queensland: A S.W. China: A India: A B Manipur: A B D Burma, North: A B D (and transovarial transmission established) Burma, Lower: A D (?)
Schöngastia schüffneri	Sumatra	Sumatra: C (Exceptional case recorded by Walch)

Legend to Table I

A: Epidemiological evidence only (seasonal incidence; coincidence of infections and infestation of man, and usually heavy infestation of local rodents, in typhus 'islands').

B: Strains of Rickettsia tsutsugamushi recovered from crushed mites.

C: Found attached to man, later an eschar appearing on the same site, followed by an attack of scrub typhus; or, found attached to man, fever following within normal incubation period after.

D: Has given infection by attachment to laboratory animals.

References to Table I

New Guinea and S.W.P. area records for T. fletcheri = T. akamushi and T. walchi = T. deliensis, in Kohls, Armbrust, Irons and Philip (1945), Blake et al (1945), Philip and Kohls (1945) and others.
Philippine records for T. akamushi and T. deliensis in Philip and Woodward (1946)
Record of T. deliensis in S.W. China by Millspaugh and Fuller (1947)

2. The Biological Relationships of Trombicula deliensis

(1) Geographical Distribution

One striking feature of T. deliensis is its very wide dispersal, from Queensland to the Philippines, and from India to the Maldives. If T. akamushi is regarded as a form of the same species, the distribution of the two forms and their intermediate varieties is extended northwards to Japan. No other trombiculid mites in the Far East has a comparable distribution.

(2) The Relationship between T. akamushi and T. deliensis

As a result of the study of a series of specimens collected in Malaya, Gater (1930) considered that T. deliensis was a variant of T. akamushi. Developments in the systematics of these mites in recent years would suggest that this view is correct, and that the two named species are extreme forms of a single polytypic species. This was supported during investigations in Imphal by the confusion of T. deliensis with at least three closely similar forms, and elsewhere by the number of species described as vectors* and later proved to be local forms of T. deliensis or T. akamushi.

* Namely, T. fletcheri Womersley and Heaslip 1943, and T. obscura Womersley 1944, from New Guinea and adjacent islands, now considered synonymous with T. akamushi; and T. fulleri Ewing 1945 from North Burma, and T. walchi Womersley and Heaslip 1943, from the Pacific theatres, synonymous with T. deliensis. Wharton (1946) has rightly stressed the importance of the "tsutsugamushi group".

Since writing the Appendices, attention has been drawn to an interesting account by Philip and Woodward (1946) on mites collected in the Philippines, where T. akamushi, T. deliensis and intermediate forms occur. They state that "in certain geographic locations the respective mite populations of akamushi and/or deliensis are relatively constant and usually assignable by known taxonomic standards, whereas in some localities including the classical endemic areas in northwestern Honshu, the characters become mutable, and very confusing." Later they make a very significant statement with which our observations are in full accord: "It appears that these species may belong to a complex of recent evolutionary origin."

(3) Larval Populations and Turnover

Not only is T. deliensis widely distributed but it is frequently the most populous species wherever it occurs. In the Imphal area during the monsoon, it was not uncommon to find 70 to 90 or more per cent of rats infested with this species, with an average of some 100-200 larvae per infested rat, and in a heavily infested site this rate of infestation might be maintained for some 4 months. Appendix 3:8ff. Figs. 3:1,3.

Different species were found to remain attached to their hosts for different periods. A short feeding time of 2-4 days appears to be shared by members of the Trombicula generic group, for it obtains not only with T. akamushi and T. deliensis in the Far East, but also with T. autumnalis in Europe, and Eutrombicula alfreddugesi and E. batatas in America. Observations in Imphal based on the larval light-trap suggest that two species of Ascoschongastia* feed for a week or more, while Wharton (1946) has reported a similar period for A. indica (Hirst). Species of Walchia, and Schöngastiella ligula in Imphal apparently fed for some 4 weeks or more. The number of feeds in unit time, for Trombicula, Ascoschöngastia, Walchia and Schöngastiella is roughly in the ratio 8:4:1:1.

By applying these figures to the overall figures for rate and intensity of infestation of rats trapped over a wide area in different areas near Imphal, we may calculate roughly the total overall annual turnover of larvae per "average" wild rat necessary in order to maintain the infestation actually observed in the field. Appendix 3:3 Fig. 3:5

This annual turnover comes to be roughly 3000-4000 larvae of T. deliensis, 700-800 larvae of Ascoschöngastia species, 200 of S. ligula and only some 50 of species of Walchia per wild rat.

It is thus clear that because of the relatively short feeding time, the actual population and turnover of larvae of T. deliensis is even greater than the heavy infestations observed on hosts would lead us to believe. It appears probable, from a study of the infestation figures in the Imphal area, that in many populous colonies of wild rats the turnover of T. deliensis may well amount to some 5,000 larvae per rat per annum. As discussed in Appendix 3 (page 9(f) this high rate of turnover has many important implications which, it is suggested, at once place T. deliensis at a special advantage which is clearly connected with its efficiency as a vector.

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* Ascoschöngastia kohlsi Philip and Woodward and A. mutabilis (Gater)

These implications may be summarised as follows:-

Appendix 3:4

The great number of separate acts of feeding represented by the above figures is related to the following:

(a) Increased opportunity for dispersal, reflected by the occurrence of T. deliensis in large numbers over a very wide geographical range.

(b) The Opportunity for the evolution of a group (the 'tsutsugamushi group') of polytypic species, and, indeed, for the emergence within this group of a species as biologically successful as T. deliensis itself. It is interesting to compare this situation with that of Rattus rattus, the principal host in the same theatre and likewise a polytypic species with a large number of named forms and innumerable intermediates.

(c) The opportunity for the perpetuation and dissemination of tsutsugamushi infection transovarially acquired. "Dissemination" here implies the scattering of numbers of infected siblings by their hosts.

(d) The opportunity for encouraging the infection whenever a colony of wild rats remains on an infected T. deliensis "island" long enough for rats to be repeatedly infested while harbouring the rickettsiae in tissue accessible to the mites - provided mites can pick up infection from rats, an important possibility which has not yet been demonstrated but is considered probable.

(e) The opportunity for the rickettsia itself to have become adapted in the past to life in mites of the "tsutsugamushi group" and their principal hosts.

(f) Finally, attention is focussed on the universal importance of a restricted group of mites which are considered responsible for most of the tsutsugamushi enzootic amongst the rats and other hosts, reflected by the transmission of infection to man by two very closely related species, and also occasional mites of other species which have happened to pick up infection encouraged by the major vectors (see below).

(4) Relationship with the Hosts

The trombiculid mites bear a triple relationship with their hosts, namely, host preferences on the part of the mites, and dispersal and encouragement of the population of mites by their hosts. The latter factors, related to the population, habitats and behaviour of the hosts, are discussed later (page 38).

T. deliensis does not appear to have very marked preferences and will even attach to an unnatural host such as man. Nevertheless, it was found that although common on all local species of rat, as well as bandicoots, shrews, tree-shrews and squirrels, T. deliensis was seldom found on mice in Burma and the Imphal area.

A number of observers (including members of the USA Typhus Commission and the writer) have noted that T. deliensis appears to be reluctant to attack man and, for example, does not appear readily on the boots although many larvae may be found if a rat is exposed on the same site. T. akamushi however would appear to attack man more freely, and Japanese workers describe it as attaching to man "with alacrity". This difference in behaviour between T. akamushi and T. deliensis is probably the explanation of Gater's observations

Appendix 3:11

(1930) that whilst T. akamushi was the common mite found attached to coolies, T. deliensis was much more common on the rats.

3. The Life Cycle of the Vector in Relation to Scrub Typhus

(1) Non-parasitic phase Nymphs and Adults

Appendix 21:1

(a) General account. It is now known that the nymphs and adults of T. deliensis and other trombiculids are not vegetarian but predaceous. They appear to be able to complete their development and lay eggs in a great variety of soils, and although the optimum conditions are not yet

known it appears that the most favourable soils are loams that are not very acid or overloaded with raw humus. Many mites (e.g. T. acuscutellaris and some scrub-itch mites) appear to be restricted in their habitat because the nymphs and adults thrive in swampy of chalky soils, or make particular environmental demands, but T. deliensis at least appears to be facultative, which partly explains the wide distribution of this species. Appendix 3:5

(b) Seasonal behaviour. Nymphs were found to become quiescent in dry soil. As discussed in Appendix 3 (page 5), moisture appears to be essential for the appearance of larvae of T. deliensis and according to the observations of Japanese workers this is due to seasonal oviposition on the part of the adults rather than to "overwintering" of the larvae or the larva-nymph resting stage. Appendix 3:5; Nagayo et al 1923; Kawamura and Ikeda 1936

During the dry season (December 1945 to March 1946) in the Imphal area, the larval population of T. deliensis appeared to be less than·5 per cent of that during the latter part of the monsoon (September to November 1945). The seasonal incidence of the disease is marked, and follows closely the seasonal appearance of the larvae during the rains. Appendix 3:8 (Table III) Fig. 3:3

Even in extremely dry weather, however, a larval population may be maintained in areas such as the seepage shown in Photo 3:8 where the soil is kept moist by ground water. This is of obvious practical importance. Appendix 3:5(1d)

In equatorial climates, the seasonal incidence of the disease would not be apparent for the simple reason that there are no seasons, although there may be fluctuations related to seasonal fluctuations in the population of hosts. Appendix 3:7

(c) Fluctuations in population. It appears probable that, in monsoon climates with a moderate rainfall, larvae may appear in a succession of waves which adumbrate the first sharp peak of incidence at the beginning of the rains. The interval between the waves corresponds to the completion of a life-cycle by batches of larvae. This appears to produce a secondary peak in scrub typhus casualties some 2-2½ months after the first rise in cases early in the monsoon. Appendix 3:10

(2) Parasitic Larvae (see also (b) and (c) above)

(a) Important hosts and potential reservoirs

The chief host in the Imphal area was a local representative of Rattus rattus brunneusculus Hodgson, a pale-bellied brown rat first described from Nepal, and common in village and camps as well as scrub and forest. Shrews (Suncus coeruleus Kerr and S. griffithi Horsfield), the tree shrew (Tupaia belangeri belangeri Wagner) and squirrels (Callosciurus pygerythrus Geoffrey and others), as well as several rats, including varieties of Rattus rattus, were also common and important hosts. Appendix 5:7

In South and Central Burma, and the Upper Chindwin area, Rattus rattus (Linn) and the bandicoot (Bandicota bengalensis (Gray and Hardwood)) appear to be the chief hosts. Appendix 1:6

Photo 1:7 of the Assam Tree Shrew (Tupaia belangeri belangeri Wagner), an important host, gives an interesting early record of trombiculid mite infestation.

Appendix 5:6

Probably all hosts which are fairly populous and freely infested are of epidemiological importance, and these fall into two categories:

(i) Potential reservoirs of infection (the possible infection of mites from hosts being assumed), for which purpose the locally common murid, frequently of the genus Rattus, would be the most efficient because of its vast population and a tendency to form compact wild colonies, and

(ii) Hosts which may carry mites, and consequently infection, over considerable distances: such would be barking deer and monkeys, both found freely infested by T. deliensis around Imphal, and also many birds, such as the crow-pheasant Centropus, which workers in several theatres have found freely infested by vector mites. The potentialities of the latter group as itinerant "reservoirs" are of course unknown.

(b) Influence of hosts on the population of mites

The larvae are ectoparasites of small mammals, and their number and distribution are naturally related to that of their principal hosts.

Appendix 3:12:15

Appendix 3:12

Appendix 3:13

Two field experiments showed that a raised rat population in a restricted area, if it is maintained for some time, may lead to an increase in the mite population. One of these experiments showed that there was rapid and significant increase in the free-living larvae on the ground as the rat-infested perimeter of a camp was approached. In Appendix 3 (see Fig. 2:60) evidence is adduced that the endemicity of scrub typhus has been increased on a number of occasions as a result of the artificial encouragement of rats in camping areas or plantations.

Appendix 6:7

There are certain practical applications concerned with the relationship between mites and their hosts:

(i) As larvae which have recently started feeding have been found to reattach to another host if their feed has been interrupted, there is some danger in killing off rats during the typhus season without taking the obvious precautions to avoid infection of man by liberated larvae.

(ii) As a high rat population encourages a heavy infestation of the ground by mites, and as the rats themselves perform the important service of "mopping-up" their parasitic larvae, an enthusiastic rat campaign, by disturbing the balance between host and parasite and increasing the number of free questing larvae, might for a time greatly increase the danger of scrub typhus infection.

(iii) The endemicity of scrub typhus may be increased wherever rats are encouraged and the ground within or around camps, gardens, plantations or compounds neglected. Reoccupation of abandoned and neglected sites is often dangerous.

(iv) It is possible that regular fluctuations in the populations of the small mammals, particularly rats, in equatorial climates may lead to regular fluctuations in mite populations and consequently to fluctuations in typhus risks which may be predictable. Appendix 3:7(3)

(v) An understanding of the favourite haunts and habits of rats and other small mammals may be applied to any study of the distribution and ecology of scrub typhus. This is of considerable help in either survey or the framing of advice on the avoidance of infection.

(c) Influence of hosts on the distribution of mites

The influence of the hosts on the distribution of the mites also has most important applications, particularly as infection in the mites can be passed on transovarially. Appendix 3:13

Trombiculid mites must actually be introduced to any patch of ground by a suitable host, and in the field a situation arises where numbers of engorged larvae tend to be introduced to the ground in scattered foci related to the behaviour of the local hosts. Added to this is a tendency for a species of mite to be dispersed more and more widely from any centre to which it is introduced. This dispersal is most efficient in T. deliensis because the larvae finish feeding quickly, and it takes place in two ways: (i) through the overlapping of territories occupied by individual small mammals, and (ii) in a disjunctive manner by transportation on hosts which travel afar. In practice it would appear that the mites are at first limited to small and scattered patches, or colonies or "mite islands", which in the course of time multiply and spread as the particular species becomes established. In suitable conditions, the mite-islands may become confluent and a large area may appear to be infested unevenly throughout. Fig. 3:11 shows an example of a stage in the expansion of two clearly recognisable mite-islands, which overlapped for some 200 yards at the place transected in this particular field experiment. The birth and distribution and development of mite-islands is open to scientific study, which has already borne fruit in a better understanding of the relationship of scrub typhus to terrain. Appendix 2:32-33 Appendix 2:32(9:10)

It is considered that ecological barriers, which interrupt the overlapping of territories occupied by individual hosts, and which have for example even been found to separate distinct subspecies and species, also serve as barriers to the spread and establishment of trombiculid mites and hence of scrub typhus.

The Indo-Burmese mountain range has apparently served as a barrier to the eastward spread of both scrub typhus and the mite Ascoschongastia indica, common in Burma, while it is considered that the Arakan Yomas range has shielded the seaboard from the spread of scrub typhus, which however is infiltrating along the ecological continuity of the Kaladan river. Appendix 2:7 3:13-14 Appendix 2:18 1:10

(3) The Mite-Rat-Mite Cycle

(a) Duration of the life-cycle of T. deliensis

Appendix 21:2

By comparing K. L. Cockings' data for T. deliensis with those of Japanese workers for T. akamushi, the life-cycle of the former would appear to be completed in some 7-9 weeks in optimum conditions.

Appendix 3:10

On the basis of the fluctuations in population described above, the life-cycle for T. deliensis in nature appeared to be in the neighbourhood of 10-12 weeks during the monsoon in the Imphal area and in Lower Burma. Miyajima and Okumura (1917) give figures suggesting 15 weeks, and Nagayo (1923), 6-7 weeks, for the life cycle of T. akamushi in the laboratory, although Kawamura and Ikeda (1936) would extend this to several months.

(b) The Mite-Rat-Mite Cycle and "Typhus Islands"

It is considered that scrub typhus develops in relation to the intensity and duration of the mite-rat-mite cycle, although the rat may be accompanied or even replaced by some other small mammal capable of acting as a "reservoir".

This would obtain even if infection in the mites were always transovarially acquired. It is however extremely probable that a small proportion of mites feeding on infected hosts can pick up the rickettsiae and thus start new lines of infected mites. Compact colonies of infested rats would then be of the greatest importance in encouraging the disease and forming centres of incubation, as it were, from which the infection may be introduced to neighbouring colonies.

Appendix 3:3

Evidence was gained during the team's investigations that in a heavily infested "island" of T. deliensis the turnover in larvae of this species may often amount to several thousands attaching to an "average" wild rat per annum.

It is stressed that the introduction of T. deliensis (or any other mite) and of Rickettsia tsutsugamushi to any site are two distinctly separate events. The patchy distribution of the disease is particularly related to

(i) the patchy distribution of the mites in "mite-islands",

(ii) the chance introduction of infection,

(iii) the inconstant occurrence of a state of affairs favouring an intense local mite-rat-mite cycle.

The phrase "typhus islands" is used to emphasise the way in which the disease is restricted to areas which may be very small indeed.*

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* For example, note the infested clump of grass in a native garden in the Pescadores, Fig. 4 in the illustrations to the Supplement to Appendix 2 (described in page 44 of the text).

The phrases "typhus islands" and "mite-islands" were used by the writer in a report on scrub typhus in Ceylon dated February 24th, 1944, and were derived from a description by Ewing (1923) of the habitat of T. tlalsahuatl in America: "In the more humid Southern parts of its range the mite is found wherever there is rough growth of weeds and shrubbery. Towards the northern limits of its range the species occurs only in isolated "islands" where the local conditions are favourable for its maintenance."

Both the endemicity and the extent of typhus-islands fluctuate, quite apart from any seasonal change, and these fluctuations may be great. Evidence for this was gained from several sources during investigations in Manipur and Burma, while Nayago (1923) remarks how the endemic areas in Japan change from year to year, sometimes appearing to travel down the rivers. Appendix 3:13

The reasons for the sharp localisation and the fluctuations in endemicity and extent of typhus islands are likely to be found in the restricted range of an adult and larval mites themselves; the restricted range of the chief or "reservoir" hosts; the need for a sufficient overlap of suitable mite and host habitats to ensure a local mite-rat-mite cycle; the population of hosts; the chance introduction of both vector mites and the rickettsiae; and the changes which the whole picture presents from year to year.

4. The Trombiculid Mites and Tsutsugamushi Infection

(1) Alternative Inter-murine Vectors and Animal Reservoirs

To Table I should be added four species of trombiculid mites (Table II) from which, according to reports, tsutsugamushi infection has been recovered. These reports must however be confirmed with laboratory-reared mites, for any worker with mites will doubt that Nagayo and his co-workers, for example, could assume that 1,400 larvae injected into a monkey belonged to one species, T. scutellaris.

Table II: Tsutsugamushi Infection in Other Species of Trombiculid

Trombicula scutellaris	Japan	Nagayo et al (1919)
Trombicula pallida	Japan	Nagayo et al (1927)
Trombicula intermedia	Japan	ibid.
Schöngastiella ligula	Ranikhet, India.	Possible infection: Kalra (Appendix 17 III)

It is well recognised that tsutsugamushi infection is essentially one of small wild mammals, the infection of man being accidental. If attention is confined to those vectors which bite man, then a faulty perspective is likely to be gained. It is to be expected that species of trombiculid mites exist which act as efficient or inefficient vectors of tsutsugamushi infection amongst their natural hosts but which do not happen to attack man. The epidemiological importance of possible inter-murine vectors was stressed by the writer in an earlier report (1944).

It is an interesting conjecture that the pre-eminence of T. akamushi and T. deliensis as vectors is related to the very large populations of these mites and their considerable turnover, and again related to the facultative nature of both the adults and the larvae, the latter attacking a great variety of hosts. This freedom to attack many different hosts accounts for the occasional and

apparently reluctant inclusion of man. It is therefore no strange accident that what appears to be the most efficient vector of tsutsugamushi is also one of the relatively few species of mite which happens to attack man.

A question of critical importance is clearly the ability or otherwise of the vectors to pick up infection from a host such as a rat. If this is possible, as is very likely, then attention should shift from the species which bite man to whatever locally numerous species exist capable of transmitting infection to, and picking it up from the hosts; for the intensity of infection amongst the man-biting species will be related to the intensity of the enzootic. As suggested in Appendix 3, it may readily be that T. pallida and T. palpalis together are of equal or even greater epidemiological importance, at least in some parts of Japan, than is T. akamushi, for the latter exists in such relatively small numbers that it might be unable to encourage sufficient infection amongst the hosts to maintain an appreciable boosting of newly-acquired infections amongst the mites. A similar situation might obtain in Kuala Lumpur (Lewthwaite, 1930), where T. deliensis is more common on rats but bites man less freely than does T. akamushi.

Appendix 3:11

Gater (1930)

In any case, for a mite to pick up infection from a host cannot be a very common event, or the infection would be almost ubiquitous.

In an effort to investigate this problem, Major Kalra first studied the course of infection in the common wild rat of the Imphal area (Rattus rattus brunneusculus Hodgson), and later attempted to infect T. deliensis experimentally. He found that the rats suffered in no way after experimental infection with R. tsutsugamushi by the intraperitoneal route. Rickettsiae could however be recovered from the blood within 24 hours, and at varying intervals up to 74 days, while recovery from the brain was possible after at varying intervals up to 99 days. Rickettsiae reappeared in the blood for several weeks after reinfection six months later. As suggested by the writer in an earlier report, if the rat can act as a reservoir it probably does so only temporarily. Kalra's findings are of considerable interest in this connexion.

Appendix 12:9(IV) 17:1(I)

Rep.5, 15 Jan.45.

Attempted Experimental Infection of Trombicula deliensis

Larvae of T. deliensis were allowed to feed for 24 hours on specimens of Rattus rattus brunneusculus infected in the laboratory and in the rickettsaemic stage, as described by Major Kalra in Appendix 12 (page 10).

Two strains of R. tsutsugamushi were recovered, but none from controls. The controls were from animals trapped on the spot, but as the only proper way to control this experiment is to work with laboratory-bred mites, the positive result is suggestive but inconclusive.

Nevertheless, the experiment showed that after 24 hours of feeding on a heavily infected rat, at which time the larvae appeared engorged, not more than some 1-2 per cent of the larvae could possibly have picked up infection, if indeed they did this at all. The lower the proportion of mites which actually pick up infection, the more important becomes the turnover, in numbers in unit time, of larvae of various species which can transmit infection between the rats.

It is worth noting that if we assume that 1 per cent of mites become infected by feeding on a rat with free rickettsiae in its blood, and that the rickettsaemic phase lasts some 70 days (see Appendix 12, page 9), then an "average" rat infected at the very beginning of the T. deliensis peak period in a highly infested area (e.g. Kanglatongbi near Imphal) might possibly infect as many as 15 mites during the rickettsaemic phase. This figure is purely hypothetical but is quoted to give a rough scale to such events.

(2) Scrub Typhus as a Man-Made Disease

It is now possible to see that during the course of evolution of the trombiculid mites a number of species have emerged which are biologically "successful" and have outstripped the other species. Of these, we are concerned with a certain number of possible inter-murine vectors and in particular with a group of closely related mites, the "tsutsugamushi group" already referred to, within which have emerged T. deliensis and its north-eastern representative T. akamushi, T. deliensis at least, if one considers its exceedingly wide distribution and its great population, is par excellence the chief trombiculid ectoparasite of rats in South East Asia.

An enquiry into the conditions which have encouraged many of the important mites shows that, in common with so many other creatures, they have been able to take advantage of altered environment created by man. For example, the chief host of the harvest-mite in Britain is the rabbit, and it is difficult to escape the conclusion that had this animal not been introduced to Britain about the twelfth century, the population of harvest mites would have been maintained, by voles and other creatures, at a much lower level. Arguing further, it is not unreasonable to suspect that should the rabbit be the principal host of T. autumnalis in Europe, then the "centre of dispersal" or home of this mite may readily have been near that of the rabbit, somewhere in south-western Europe. Similarly, the scrub-itch mite Eutrombicula batatas common in Dutch Guiana, Columbia and Panama has as its chief host the chicken, and according to Michener (1946) this species "apparently becomes abundant only in the grassy areas around houses and in villages where domestic animals, particularly chickens, are numerous." This species has clearly been encouraged by man.

The natural vegetation in all scrub-typhus countries is forest, in which small mammals are usually arboreal. It is contended that by clearing forest tracts for primitive shifting cultivation, man has greatly encouraged the vectors of scrub typhus, firstly by growing foodstuffs and so promoting the rat, and secondly by removing the canopy and bringing the rats down to the ground, which condition apparently favours the life-cycle of many trombiculid mites. In this way, man has encouraged a low grade enzootic wild infection, "jungle" or "sylvatic" tsutsugamushi, to develop into epizootic intensity, producing an endemic disease which is still in process of extending and establishing itself. Appendix 2:34-38

This disease involves rats and their ectoparasites, and its dynamic aspects are sufficiently impressive to suggest that scrub typhus is of more than academic interest. Appendix 2:38

At a conference held on February 3rd, 1944, at Ceylon Army Command H.Q., it was suggested by the writer that scrub typhus may be a "man-made" disease, to be ranked with "man-made malaria" as a consequence of man's interference with natural balances.

In a later report (No. 11 dated October 1945), it was surmised that the akamushi-deliensis group of mites, together with the rats which are in a way parasites on man's homesteads and his fields, were given a particular opportunity in life when tracts of jungle were cleared by primitive man for cultivation and occupation; and that they have gradually spread and multiplied while their rickettsioses have followed behind, presumably being boosted whenever conditions allowed a heavy infestation of suitable mammals in the presence of the infection. Further, it was contended that the occasional vectors which had been suspected by various workers may be set aside while attention is focussed on the universally important "tsutsugamushi group"; whilst of the multitude of hosts and "reservoirs" described, the Murids, and particularly the genus Rattus should be considered paramount. The alternatives should not be allowed to confuse the general picture, which involves a restricted group of closely related mites, and a restricted group of principal hosts on which the mites are important parasites.

The ecological work carried out by the Scrub Typhus Research Laboratory, described in Appendix 2, has supported this contention, that scrub typhus is largely a disease encouraged by man.

(3) An Economic Grouping of the Trombiculid Mites

It is helpful to divide the trombiculid mites into groups as follows, completing the list by appending certain gamasid mites which transmit murine or flea-borne typhus.

A. Vectors of Tsutsugamushi

(a) Vectors of Universal Importance, transmitting infection to man. These are strictly limited to T. deliensis and T. akamushi, both polytypic members of the "tsutsugamushi group" of Nagayo and other workers.

(b) Inter-murine vectors, including probably most or all members of the tsutsugamushi group (and see Table II): the inter-murine vectors are unknown but may comprise a large number, although there are some reasons for believing that some potential vectors at least are very inefficient.

Appendix 3:11

Species of Ascoschöngastia, because of their relatively large turnover and their wide distribution, may include important inter-murine vectors, which however do not bite man. If the very widespread species A. indica is a potential vector, then its presence in Burma is probably of considerable epidemiological importance.

(c) Inefficient or Exceptional Vectors. Included in the above group are mites which are either (i) inefficient vectors which however attack man freely, or (ii) more efficient vectors which rarely attack man, but which may act as occasional vectors to man. Schöngastia schüffneri in Sumatra must be included in the first of these groups, for although it is reported to attack man in large numbers in endemic areas, it is definitely not the locally important vector. The exceptional case of infection by this species recorded by Walch must, it is suggested, be considered as an occasion of a very inefficient vector which happens to have picked up infection in the presence of a heavy infection maintained by T. deliensis amongst the local animals.

B. Scrub Itch Mites

These attack man viciously and often in great numbers and are known in every continent except Africa. They do not transmit scrub typhus, and we are confident that on the whole they cannot for in certain areas nature gives them every opportunity to do so, where scrub itch occurs in endemic areas and the mites freely infest the local rodents.

The ability to transmit typhus is as mysteriously restricted amongst mites as is the ability to carry malaria amongst Anophelines.

C. Other Trombiculid Mites of no known importance to man or animal hosts.

To make this list complete we should add:

D. Parasitid (Gamasid) Mites carrying "OX.19" rickettsial strains.

The parasitid rat-mites are more closely related to the ticks than to the trombiculids: they look superficially like tiny ticks and live in the fur. There is no "soil-bound" phase corresponding to the trombiculid adults, but the mites leave their hosts between

feeds. The nymphs and adults feed repeatedly at intervals, as do bedbugs and argasid ticks. They are important vectors of a number of murine infections. Liponyssus and Laelaps are very widespread on rodents, and species of Liponyssus are known to transmit 'endemic murine typhus' from rat to rat and occasionally to man, while a related species is a vector of "rickettsialpox", a newly described rickettsial disease. Huebner et al. (1946)

When studying the natural history of "murine" or flea-borne typhus, the gamasid mites, the fleas, and murine sucking lice such as Polyplax must all be considered together. It is not unreasonable to suspect that the gamasid mites might have been concerned in the evolution of "murine" typhus, while their close relationship to ticks is interesting.

5. The Relationship of Scrub Typhus to Terrain*

From January 1944 onwards efforts were made to study the ecology of scrub typhus, so that by understanding the relationship of the disease to terrain sensible advice might be given to troops on the avoidance of dangerous sites. At the same time, it was clearly necessary to apply such knowledge to evolving methods of survey.

The relationship of the disease to terrain appears to be confusing at first sight, because it presents a variety of dissimilar facts. This is because to any consideration of the habitat of the mites must be applied that of the habitat and behaviour of the hosts: the nymphs and adults demand suitable soil conditions; the parasitic larvae are encouraged by a sufficiency of hosts while their population must be maintained by local conditions which allow the return of replete larvae to the same breeding ground. In spite of the bewildering variety in typhus habitats, however, common factors can be found and the picture is in fact fairly simple.

Because potential hosts are largely arboreal and the soil tends to be overloaded with raw humus, and for other reasons discussed in Appendix 2, forest does not apparently favour an intense mite-rat-mite cycle so much as scrub.

In the areas investigated, the heaviest concentrations of larvae of the vector T. deliensis were found in grassy scrub where there had been some fairly recent reason for a high rodent population; and also in the intermediate belt of vegetation between open scrub and forest. Outbreaks and pinpointed cases have been in similar terrain.

A study of mite and mammal ecology, and of the typhus islands described in the literature and investigated over a wide area in the field, suggests that a practical and simple classification of typhus terrain is on the following lines.

A. Broad Classes of Terrain. There are three broad classes of terrain, within which certain ecological features may particularly favour the development of hyperendemic foci.

1. Man-Made Waste Land

(a) Rural Waste Land; Abandoned clearings or "Ponzos"

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* This is described in detail in Appendix 2 pages 34-42, while illustrations from the literature are contained in Figs. 1 to 8 of the Supplement, described on pages 43-45 of Appendix 2.

(b) Domestic or "Suburban" Waste Land

(i) Domestic waste land in villages, occupied or abandoned (including abandoned camps).

(ii) Neglected plantations and native gardens.

2. Water-Meadows (grassy river banks).

3. Relict forest belts or coppices (often following water-courses).

B. Specific Ecological Features operate within these broad classes of terrain, offering particular attraction to rodents and shrews.

Appendix 2:37(C) A study of the ecology of the small mammal hosts has suggested that the intermediate zones, where distinct ecological units meet, are of particular importance. From the epidemiological point of view, the most important of these intermediate zones or "fringe-habitats" are the scrub-forest fringe of dense vegetation, hedgerows, and waterside fringe-habitats such as the rank vegetation at the edge of a stream.

Perennially moist foci are of particular importance in monsoon climates but of much less importance in equatorial climates.

The relationship of scrub typhus to terrain is summarised in Appendix 4:3 Chart I. The origin of typhus-scrub is, as has already been observed, largely a consequence of primitive shifting cultivation* and the storing of food by man.

Shifting cultivation is practised by natives in remote areas, Appendix 2:4(3) who clear forest extensively and burn the clearings during the dry season. The clearings are cultivated for one or two seasons and then abandoned for at least ten years. Meanwhile, neighbouring forest tracts are successively cleared and cultivated, so that in time the forest over thousands of square miles may become replaced by a patchwork of scrub in various stages of reversion to jungle. Patches of woodland or belts of forest following watercourses stand out in such terrain, and they then appear frequently to act as sanctuaries for small mammals. The native Burmese name for abandoned clearings is ponzo, and this term is in current use by the Forestry officials. Chart II indicates the inter-relationships between, and the origin of, the various ecological units which make up the countryside and are concerned in the ecology of scrub typhus. This Chart is derived from that on page 8 of Appendix 1, and includes references to photographs illustrating the types of terrain under discussion. It should be compared with the more detailed chart on page 35 of Appendix 2.

The suburban or domestic type of waste-land is of considerable importance: over two-thirds of all scrub typhus cases in South and Appendix 1:9 Central Burma in 1945 were contracted in domestic waste land within or on the outskirts of villages and towns. A classical example is the infected foci in native gardens in the Pescadores (see Figs. 4 Appendix 2:44 and 5, supplement to Appendix 2). This type of infected waste land owes its existence to neglect and may remain quite unsuspected in populated areas, until the inhabitants change their pattern of living or immigrants such as troops occupy them. Children are Appendix 1:9(44) however frequently exposed, and it is possible that much scrub-typhus amongst children in Burma has escaped observation in the past.

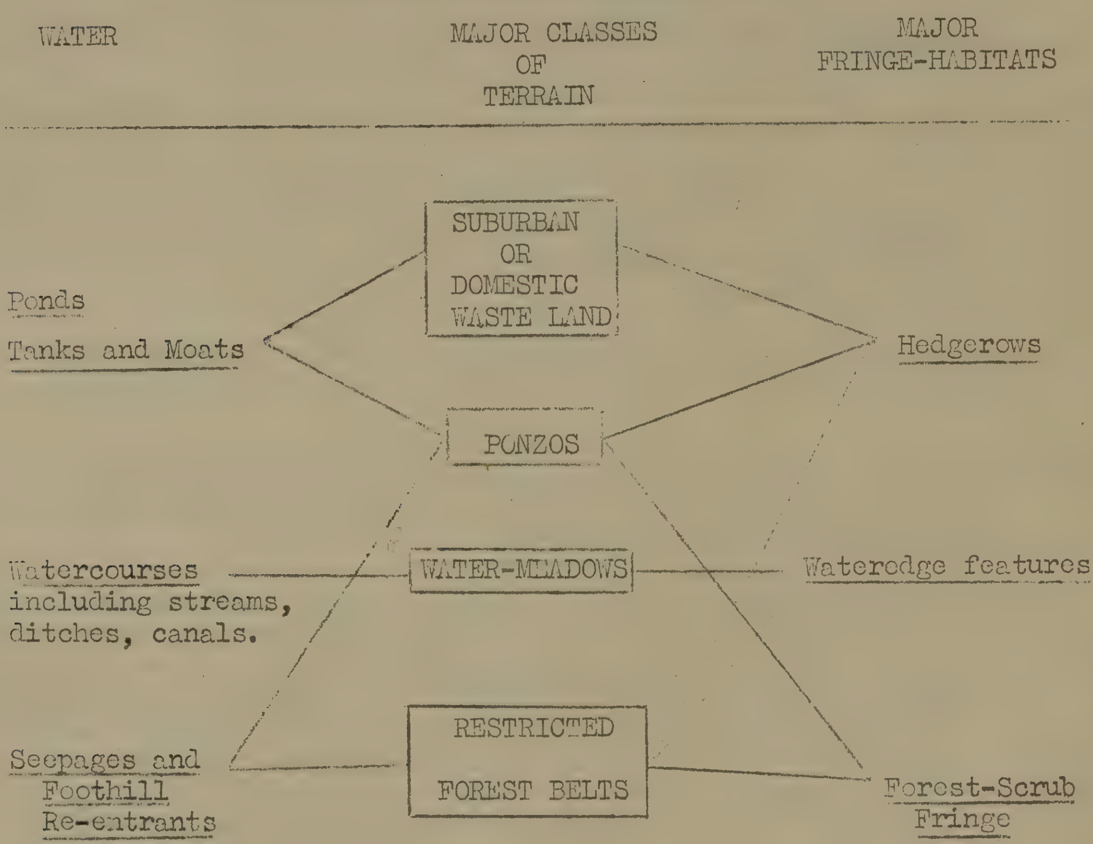
There is evidence that the encouragement of rats to camps in

* Known as chena in Ceylon, jhuming in India, taungya in Burma, caingin in the Philippines, et

endemic areas, followed by abandonment or neglect, has increased the endemicity within one or two seasons (see Fig. 2:60). This is a small-scale repetition of what has happened in classical outbreaks in Malaya and Sumatra, and it points to the human factor in encouragement of the disease.

Chart I: Typhus and Scrub

Relationship of Scrub Typhus to Terrain



Appendix
1:8

Chart II

Origin and Interrelationships of the Types of Scrub or Waste Land concerned with Scrub Typhus

Note: The classes of Scrub which contain almost all the endemic and hyperendemic foci of practical importance are underlined in the Chart. All these are considered to have derived from the original climax forest and from meandering watercourses.

The figures refer to photographs illustrating the various features.

Restricted Relict Forest Belts, often following watercourses - ← ORIGINAL VIRGIN FOREST 6,19,48 ⇄ WATERCOURSES 19,30,33

WATERCOURSES 19,30,33 ↓ WATER-MEADOWS 10,19,48,49,27

FOREST FRINGE 7,11,17/18,56 (and cf. 31,39,42) ↑

human interference →

natural interference ↑

TEMPORARY (SHIFTING) CULTIVATION

↓

Abandoned clearings

"PONZOS"
7,17,22/23, 24,25

VILLAGES & CAMPS

Abandoned Villages & Camps
27,32,43/44

Settled Villages: Domestic Waste Land within
29,32,33,34, 35,37

Neglected native gardens or plantations
43/44, 54,55

PERENNIAL CULTIVATION

↓

a. Paddy
b. Crops
c. Native gardens
d. Plantations

Neglect or abandonment

RURAL, and SUBURBAN or DOMESTIC,

MAN-MADE WASTE LAND.

6. Methods of Survey and Control

Schemes for carrying out reconnaissance and more elaborate field surveys are described in detail in Appendix 6, while the application of air photography to surveyand research is discussed in Appendix 4. Once definite information has been gained about the distribution of mites and infection in an area, methods of control will suggest themselves naturally.

Cultivation, and possibly grazing, are suggested as economical methods of control. Since writing Appendix 6, the author's attention has been drawn to a paper by Bushland (1946) in which the practical value of spraying infested ground with oil is confirmed, and a dosage is suggested of 40 gallons of diesel oil per acre, repeated at 2 day intervals. Kawamura (1926) and his co-workers also found petroleum emulsions effective in this respect.

The rationale of anti-rat measures in the control of endemic areas is discussed in Appendix 6. It is both dangerous and uneconomical to adopt anti-rat measures in anticipation of the typhus-season in monsoon climates. Prebaiting should be started in time for the maximum kill to coincide with the first peak period of infestation, a month or so after the rains start. Appendix 6:7

Field surveys are designed to collect information which falls naturally into three groups, the first being most simply obtained: Appendix 6:1-5

(a) The infestation of the local rodents and shrews: The endemicity is broadly related to the population of T. deliensis, and rule-of-thumb criteria are suggested for guidance in estimating risks.

(b) The population of free larvae on the ground: Larvae may be collected actually from the ground, and these findings correlated with the local infestation rates.

(c) The degree of active infection amongst the local hosts and the mites.

These field investigations will be facilitated by various techniques adopted or evolved by the team at Imphal:

(i) Examination of rats under anaesthesia, if it is required to keep them alive for use as bait (Fig. 5:2). Appendix Appendix 5:4

(ii) Use of local wild rats, free of infestation (or alternatively, white rats, guinea-pigs or gerbils) as bait for collecting larvae from the ground (see Photo 3:6). It is considered that all methods of collecting mites off man or inanimate objects are likely to give a totally false impression of the prevalence of T. deliensis. Appendices 5:4 6:4

(iii) The use of cardiac blood from rats, instead of emulsified viscera, as an inoculum for the recovery of infection (Kalra). This technique enables rats to be kept alive, is more simple, and also probably gives a more precise index of active transmission. Appendices 12:1(2) 6:4(3)

Appendices 21:2 19:1 6:4(3)

(iv) Freeing of larvae from debris, for purposes of identification or for inoculation, by (a) pinning ears to corks of tubes until the larvae have detached, or (b) using the light-trap devised by K. L. Cockings, or (c) floating scrapings in saline for 24 hours, as suggested by Major Kalra.

Appendix 21:2

(v) The use of the light-trap, devised by K. L. Cockings, for the collection of larvae (for identification, breeding or inoculation) the rats being naturally disinfested and left in a fit state to be used as bait.

Appendix 6:4(2)

(vi) It is worth considering using the local wild rats, which are hardy and require little attention, as temporary repositories for inocula from infected material. Such rats may be taken back to base a month or two later and their blood inoculated into white mice.

7. Salient Points in Future Research

The investigations of the research team based in Imphal have been continued, in the shape of field surveys over various endemic areas in India, by Major S. Lal Kalra (Field Typhus Research Detachment), who is of course investigating all forms of endemic typhus fever. Some of Major Kalra's recent investigations are described in Appendices 15, 16 and 17. An intensive study of the ecology of mites and rats, and hence of scrub typhus, is also to be undertaken by a team based on the Institute of Medical Research at Kuala Lumpur, under the auspices of the Colonial Medical Research Service.

It will help to orientate the preceding discussions if some of the more urgent investigations are noted. There are in addition many aspects of scrub typhus research which are of considerable biological interest.

The major problem confronting the epidemiologist is to determine if the vector larvae can pick up infection by feeding on infected rats, and if so, the various circumstances in which this obtains. The efficiency or otherwise of other prevalent species of mite as inter-murine vectors should then be studied, as it is clearly of great importance to gain more insight into the enzootic level of infection.

Both these investigations await a fully satisfactory technique for breeding mites. (By preserving the larval pelt on emergence of the nymph, it is possible to identify species during the course of breeding, a feat of great convenience and obvious importance).

The following aspects are of immediate practical interest:

(a) The course of infection in various important hosts and their potentialities as "reservoirs".

(b) Host-preferences of T. deliensis and T. akamushi and the circumstances (microclimate etc.) in which the larvae attack man.

(c) The fate of both larval and adult populations in the soil if hosts are excluded.

(d) The ecology of the predatory nymphs and adults in the soil: relationships with other predators such as bdellid mites; feeding habits in nature; influence of soil pH

and bacterial and fungal content; behaviour in layers of soil, in relation for example to accessibility to chemicals.

(e) The duration of the life cycle in nature, and the duration of larval feed for different species.

(f) Accurate data on larval and adult populations and their relationship to soil conditions and the populations and behaviour of the hosts.

(g) The ecology of the principal hosts: particular features of habitat and behaviour which encourage the life-cycle of the vector (and also of fleas and gamasid mites); rodent populations, their promotion and control.

(h) Biotic influences: a study of the manner in which rats and their ectoparasites are, and have been, encouraged by human activities.

(i) An investigation of the extent of infections in native children in endemic areas.

(j) Field experiments on methods of control.

GENERAL OBSERVATIONS ON OTHER INVESTIGATIONS

The following is a summary of a number of investigations, by members of the team at Imphal, which have not been included in the preceding discussion.

A. Clinical and laboratory diagnosis

1. Browning and Kalra summarise the clinical features of cases of scrub typhus seen at Mandalay. Tympanites was a marked feature, whilst deafness was not observed. In an outbreak elsewhere, deafness may be pronounced and tympanites absent, and it is interesting to observe that while the clinical picture is generally consistent in any particular outbreak, it may show variations in different outbreaks and in different localities. One reason for this is almost certainly variation in the local strains of R. tsutsugamushi; and the proportion of eschars is presumably also associated with the properties of particular strains. Appendix 23:1

2. The Weil-Felix reaction is discussed by Kalra, who considers that the test (a) is valueless in studying animals, (b) is not a reliable index of the endemicity of scrub typhus when applied to natives, (c) is not a reliable guide to the differentiation between the typhus fevers; and (d) the Weil-Felix titres to OXK, OX19 and OX2 did not appear to have risen significantly in a series of pregnant women examined. Appendix 13

B. Tsutsugamushi infection in laboratory animals

3. Kalra has described the behaviour of strains of R. tsutsugamushi, recovered during field investigations, in several laboratory animals (white mice, guinea pigs, and rhesus monkeys) as well as in the wild rat, *Rattus rattus brunneusculus*. He describes the stages of adaptation of the organism during intraperitoneal passage in white mice, proceeding from a stage of endothelial vacuolisation with scarce inclusion bodies and no visible rickettsiae, to a reduction in the vacuolisation and an increase in the inclusion bodies with scanty rickettsiae, and finally to a heavy rickettsial infection and a reduction in the inclusion bodies. Appendix 12:4

Kalra associates the vacuolisation with the free serious exudate of the early stages. He also suggests that the passage of rickettsiae through different laboratory animals may modify their antigenic structure and lead to atypical reactions, an observation which the present writer suggests has much to commend it.

Appendices 12:6-8

4. Experimentally infected rhesus monkeys appeared to acquire considerably varying degrees of immunity. An increase in azurophilic granules in the lymphocytes was observed in all cases, and this was also seen in blood films from one patient. Rickettsial bodies were observed in the large mononuclears.

Appendix 12:12(7)

5. From a comparison of strains of R. tsutsugamushi from different sources, Kalra concludes that they show differences in virulence and antigenic structure sufficient to account for clinical variations, including the vagarious eschar.

C. Morphology and histology

Appendix 19 & Figs.

6. Kalra has made observations on the internal anatomy of T. deliensis and has described some valuable histological techniques for such studies.

Appendix 11 & Figs.

7. The development of the nymphophane of T. deliensis is described by Thomas, who considers that the "dorsal cone" of the nymphophane accommodates the sensory hairs of the nymph. Japanese workers had considered the dorsal cone to be an organ of escape.

Appendix 19:4

8. During a study of the histopathology of the eschar and of the reaction to attachment of mites in the ears of rats, Kalra has made two interesting observations, firstly concerning the absence of traces of a stylostome or sucking-tube in eight eschars examined, and secondly in an apparent association of marked necrotic reaction in rats' ears with infestation by species of Ascoschöngastia and Walchia (but not with T. deliensis). Such observations should be continued as they may throw light on the natural hosts of the species.

D. Typhus fevers in India

Appendix 15 & Figs.

9. Kalra in a study of records for the Army in India has found that scrub typhus, murine typhus, and tick typhus are all widespread. Scrub Typhus appears to be most prevalent in Bengal, Assam, and the Himalayan foothills. In the Kumaon Hills, T. deliensis was found up to an altitude of 7,000 feet, and scrub typhus appeared to be very well established there. (In a personal communication, Kalra states that the substance of Appendix 15, on the distribution of the typhus fevers in India, is in press in the Journal of the India Army Medical Corps).

Appendix 12:3&6
Appendix 17:3

10. A strain of Rickettsia identical with or closely related to D. rickettsi was recovered by Kalra from nymphs and adults of the tick Haemaphysalis leachi var indica, taken from a rat trapped near Imphal (Palel). Similar strains, all of low virulence, have apparently been obtained from ticks in other parts of India, and these are the first records in India of an organism of the Rocky Mountain spotted fever group.

Appendix 17:6

11. Lt. Col. Pasricha in 1944 described what appeared to be an outbreak of Q-fever in Dehra Dun, while the present writer has described an isolated outbreak of an "OX2/OX19" type, clinically "tick-typhus", but with eschars, in Bhopal State in 1945. It thus appears that the African type of tick-typhus may be represented in India, as well as the Rocky Mountain type and Q-fever.

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Laboratory Establishment (Audy)

THE ESTABLISHMENT OF THE RESEARCH LABORATORY AT IMPHAL (MANIPUR),

Including Acknowledgements

1. The Situation at the End of the 1944 Manipur Campaign

The following account is intended to summarise the history of the research team based on Imphal, and also particularly to serve as an acknowledgement to the individual research workers and their assistants.

At the end of 1944, the only organised investigation of scrub typhus being carried on in the field in the S.E.A.C. theatre was in the Maldives, by Major S. Lal Kalra, IAMC, Pathologist in charge of the GHQ (India) Field Typhus Research Team, and S/Ldr. Charles D. Radford, R.A.F., an authority on mites selected by the Medical Research Council Scrub Typhus Commission.

In November, 1944, the writer was detached from anti-malarial duties with the 11th East African Division in order to carry out certain field investigations in forward areas, pending the organisation of a laboratory. In the same month, Major H. M. Thomas, B.Sc (Hons) (then Captain, R.A.M.C.) was detailed by Brigadier G. J. V. Crosby, C.B.E., T.D., M.D., then D.D.M.S. 33rd Corps, to assist in field work.

Major Thomas carried a number of burdens in the growing team and investigated the bionomics and development of the mites, as well as making contributions to various investigations and later consolidating the records. He was released in February, 1946. The writer wishes to express particular acknowledgement of his support.

Mr. K. L. Cockings, Friends' Ambulance Unit, was originally intended to be Dr. Kenneth Mellanby's assistant, preceding him with certain equipment to arrive in Imphal in January, 1945. After assisting in the early field work and later also attending to the unit transport, he took over all the breeding of mites, devised a most useful mite trap, and made a start in the important work of correlating new species of larvae with their nymphs and adults, until he left Imphal in early January, 1946.

2. The Scrub Typhus Research Team in early 1945.

The War Establishment of the Scrub Typhus Research Laboratory, an ALFSEA unit, was approved with effect from the 14th March, 1945, and mobilisation was started two months later. Much equipment had however already arrived in Imphal in anticipation.

After six months of work in Addu Atoll, the G.H.Q. (India) Field Typhus Research Team (Major S. L. Kalra, I.A.M.C., Pathologist, Sgt. J. D. Bower, R.A.M.C., Jemadar Katar Singh, I.A.M.C., and 3 I.O.Rs.) and S/Ldr. Charles D. Radford, R.A.F., and his assistant Pte. J. Hake, R.A.M.C. arrived in Imphal between the 8th and 13th April.

The GHQ (I) Team remained throughout, Major Kalra carrying out the bacteriological, serological, and histological investigations of the whole team.

S/Ldr. Radford (April to September, 1945) has published a paper describing the trombiculid mites found in the area between January and the time he left. Most members of the team studied the systematics of these mites under his guidance, particularly W/O Ash and Sgt. Lawrence.

F/Lt. A. A. Bullock, D.Sc., R.A.F.V.R., a botanist who had been selected by the Medical Research Council and sent out from the U.K., joined the team on May 9th, and started systematic botanical investigations. It had already been decided to take as a representative area the district of

Kanglatongbi, between 15 and 25 miles North of Imphal on the Manipur road. There had been an outbreak and a number of sporadic cases in this area, and Trombicula deliensis had been found infesting rats caught in an infected camping area at mile 117 in November, 1944. There was a mosaic of vegetation associations there, and a river, while it was within easy reach of the base Laboratory. F/Lt. Bullock left Imphal on the 10th March, 1946.

3. The Full Development of the Team in the second half of 1945.

Major M. L. Roonwal, Ph.D., specially seconded from the Zoological Survey of India to the GHQ (A) Field Typhus Research Team, joined it on the 30th June, and worked on the zoology of the Kanglatongbi area in collaboration with F/Lt. Bullock until he left on 3rd January, 1946, for the Z.S.I. to study his collections. Jem. Katar Singh, after a course in taxidermy at the Z.S.I., was attached to Major Roonwal by Major Kalra as his personal assistant, until the former left the area.

Dr. H. C. Browning, Ph.D., selected by the Medical Research Council, arrived from the U.K. in June, bringing a thousand mice. He was joined on 5th August, while investigating an endemic area at Mandalay with Major Kalra, by Mr. T. Gordon who brought a thousand more mice from the U.K. Dr. Browning, assisted by Mr. Gordon, worked throughout in close collaboration with Major Kalra, using the mice, and later native rats as bait for investigating mites and infection in situ. His work was interrupted by an attack of malaria and later a bout of scrub typhus contracted in a sharply pinpointed area in the mountains above Palel: from this site, a strain of Rickettsia tsutsugamushi was recovered from Dr. Browning himself, 5 strains from two species of rat, a tree shrew and a field mouse, 4 strains from pools of mites including T. deliensis, and one different strain from ticks. It was a thorough demonstration of a typhus "island". Dr. Browning left Imphal on the 23rd December.

Captain H. C. Steward, R.A.M.C., joined the team on 24th May as a non-technical general duty officer, taking on the main burden of administration and quartermastering. He left on 10th March, 1946.

With the research programme as envisaged in March, 1945, a medical officer on the establishment of the ALFSEA Laboratory would have been detached, in time, to take over a Field Team to be based in Meiktila (Burma), later in Malaya, and to work in close contact with the troops. Unfortunately this important detachment never materialised. The situation had changed completely by the middle of the typhus season, and shortly after Captain W. Stanbury, R.A.M.C., joined the unit on November 11th, it was decided that the detention of a worker of his competence for the few remaining months, when only long-term lines of enquiry remained open to him, would be uneconomical. Captain Stanbury was accordingly posted to the District Laboratory in Calcutta in January, 1946. In collaboration with Major Kalra, he had started investigations which were later abandoned.

Dr. R. Lewthwaite, O.B.E., Field Director of the M.R.C. Typhus Commission, visited the team in Imphal from the 2nd to the 14th September, while Dr. Kenneth Mellanby, O.B.E., Deputy Field Director, was with the team from June until September, including a visit to Mandalay and two to the U.S.A. Typhus Commission at Myitkyina in his stay.

4. The Contribution of British Other Ranks.

The work of the B.O.Rs. in the team deserves special mention. The importance of the B.O.R. in research work, and, especially in field work, of the trained reliable I.O.R., is much underrated. There was for example a tendency for this particular research team to be top-heavy in research officers with insufficient support by B.O.R. and I.O.R. assistants, until towards the end of the team's services.

Sgt. J. D. Bower, R.A.M.C., was Major Kalra's personal assistant throughout, and accompanied him on field surveys.

Sgt. J. Hake, R.A.M.C., who came over with the team from Addu Atoll, remained throughout in charge of the routine trapping and collecting, proving himself a great enthusiast. He left Imphal in March, 1946.

Cpl. J. Rees, R.A.M.C., was with the unit from May to November, at first engaged in field work, later being attached to Dr. Browning and taking most efficient charge of the laboratory animals. This task was then taken over by Cpl. E. Brown, R.A.M.C. (October, 1945, to January, 1946) who with Sgt. T. Raine (May to November, 1945) worked also in the unit workshop, and maintained unit transport.

W/O G. W. Ash, R.A.M.C., selected from an East African Malaria Section, was in charge of the mite laboratory, at first under S/Ldr. Radford, from 25th May until he left on 17th September to start a survey in Burma. He was released on the 10th November.

Sgt. T. J. Lawrence, R.A.M.C., was posted on 27th July and his release was deferred until March, 1946. He also worked at first under S/Ldr. Radford, and took over the entomological work from W/O Ash, making most useful contributions in this sphere.

Sgt. W. K. Ford, M.Sc., R.A.M.C. (Entomologist to the Liverpool Museum) arrived on 13th November and remained with the unit throughout. He also worked on mite systematics, and took over the routine identifications while Sgt. Lawrence prepared descriptions of the species newly encountered after Radford's departure.

Sgt. R. Finnimore, R.A.M.C., was with the unit as Clerk from 24th August until the unit disbanded.

Sgt. J. E. Linder, R.A.M.C., arrived on 28th August, and was attached to Major Kalra for histological work, in which he proved a great asset. He was deferred until January, 1946.

Finally, Sgt. N. Kennedy, R.A.F., was attached as a personal assistant to F/Lt. Bullock from October, 1945 until he was released in January, 1946.

Until the 15th October, when the permanent staff of I.O.R's arrived, the team worked with the assistance of batches of Indian Pioneer Corps personnel, who unhappily were frequently changed; their enthusiasm deserves commendation.

5. Extension of Investigations into 1946

By the 15th January, 1946, the whole of the Manipur area and the Kabaw-Kale valley had been evacuated of troops, but arrangements had been made for the remnant of the team to continue investigations in isolation until the end of March. This extension, which completed the dry season, and was sanctioned with considerable foresight, proved very profitable indeed.

The Scrub Typhus Research Laboratory, an ALFSEA unit, reverted to GHQ (I) on April 1st and was disbanded on 30th June, 1946. The GHQ (I) Field Typhus Team continued field investigations on tick and scrub typhus in India shortly after that date. The O.C. Scrub Typhus Research Laboratory arrived in the U.K. on 14th August and was granted accommodation and many facilities in the Department of Entomology of the London School of Hygiene and Tropical Medicine, until the present consolidated report on the team's work was completed and edited.

6. Specific Acknowledgements

We are particularly indebted to Lieut. General T.O. Thompson, C.B., C.B.E., K.H.P., for his great encouragement and enthusiastic support of the research laboratory, and also to Dr. R. Lewthwaite, O.B.E., Field Director of the M.R.C. Scrub Typhus Commission. Our thanks are also due to Colonels B.L. Taneja, J.J. O'Dwyer, C.B.E., and M.H.P. Sayers, O.B.E., for their constant encouragement and advice, and to Major General W.E. Tyndall, C.B., C.B.E., M.C. for supporting an extension of the research programme into 1946.

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7. Acknowledgements - Assistance during the course of field investigations

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The labour of completing this Report has been greatly lightened by the efforts of Mr. W.H. Rigglesford, O.B.E., C.6(c) (Reproduction) and Miss E. Zemla, C.6 (Type Section) of the War Office, and their staffs whose patient co-operation is acknowledged.

SUBJECT INDEX

The following alphabetical index to subjects in Parts I, II and III of this Report gives three types of reference:-

(1) References to the Reviews in Part I are given, e.g., "P.3". The treatment of the subjects is usually of a general nature, but further (marginal) references are often included in the text.

(2) References to the Appendices (Part III) are given in the form, e.g., "2:4" (Appendix 2, page 4), or "2:4(3)" (Appendix 2, page 4, section 3 of the text), and should the subject be contained in a Table or Chart, this is noted in parenthesis, e.g., "1:2(2)(Tables)" (Tables I and II, section 2 of page 2, Appendix 1).

(3) References to the Illustrations to the Appendices (Part II) are contained in parenthesis. The legends to the Illustrations may be of importance, particularly in Appendix 2, and reference should always be made to these. As a guide to the important legends, the following pages should be consulted:-

Appendix 1: Page 1

Appendix 2: Pages 20 to 31, and also 43 to 45 (Supplement)

Appendix 3: Pages 17 to 18

Appendix 11: Pages 4 to 5

ADDENDA TO SUBJECT INDEX